

06/20/2005 10783325.trn

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LOGINID:SSSPTA1626GMS

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
 NEWS 2 "Ask CAS" for self-help around the clock
 NEWS 3 FEB 28 PATDPAFULL - New display fields provide for legal status
 data from INPADOC
 NEWS 4 FEB 28 BABS - Current-awareness alerts (SDIs) available
 NEWS 5 MAR 02 GBFULL: New full-text patent database on STN
 NEWS 6 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded
 NEWS 8 MAR 22 KOREAPAT now updated monthly; patent information enhanced
 NEWS 9 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS 10 MAR 22 PATDPASPC - New patent database available
 NEWS 11 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS 12 APR 04 EPFULL enhanced with additional patent information and new
 fields
 NEWS 13 APR 04 EMBASE - Database reloaded and enhanced
 NEWS 14 APR 18 New CAS Information Use Policies available online
 NEWS 15 APR 25 Patent searching, including current-awareness alerts (SDIs),
 based on application date in CA/CAPLUS and USPATFULL/USPAT2
 may be affected by a change in filing date for U.S.
 applications.
 NEWS 16 APR 28 Improved searching of U.S. Patent Classifications for
 U.S. patent records in CA/CAPLUS
 NEWS 17 MAY 23 GBFULL enhanced with patent drawing images
 NEWS 18 MAY 23 REGISTRY has been enhanced with source information from
 CHEMCATS
 NEWS 19 JUN 06 STN Patent Forums to be held in June 2005
 NEWS 20 JUN 06 The Analysis Edition of STN Express with Discover!
 (Version 8.0 for Windows) now available
 NEWS 21 JUN 13 RUSSIAPAT: New full-text patent database on STN
 NEWS 22 JUN 13 FRFULL enhanced with patent drawing images
 NEWS 23 JUN 20 MEDICONF to be removed from STN

 NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
 MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
 AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

 NEWS HOURS STN Operating Hours Plus Help Desk Availability
 NEWS INTER General Internet Information
 NEWS LOGIN Welcome Banner and News Items
 NEWS PHONE Direct Dial and Telecommunication Network Access to STN
 NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that

specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 11:38:58 ON 20 JUN 2005

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 11:39:27 ON 20 JUN 2005

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 JUN 2005 HIGHEST RN 852520-85-5

DICTIONARY FILE UPDATES: 19 JUN 2005 HIGHEST RN 852520-85-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Crossover limits have been increased. See HELP CROSSOVER for details.

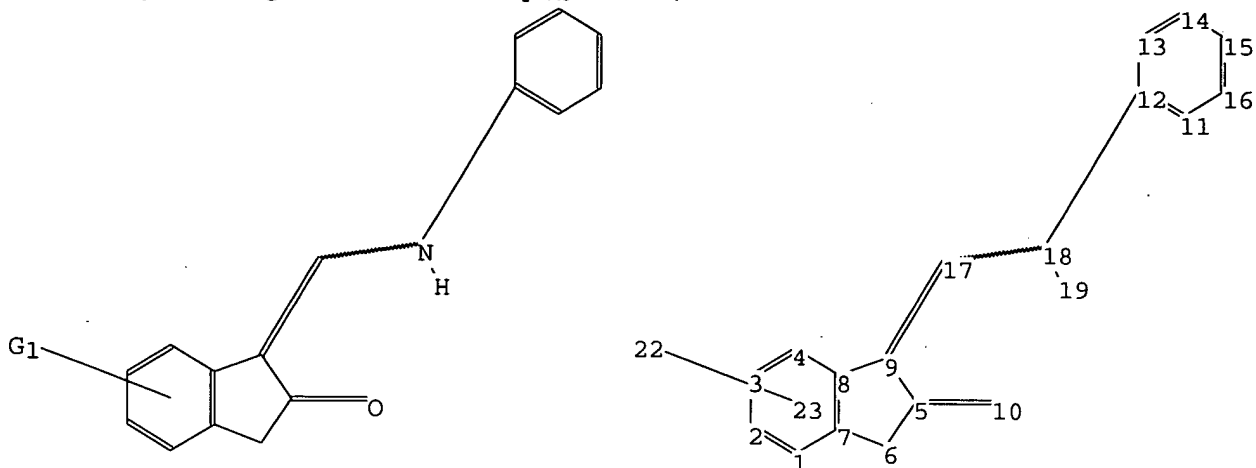
Experimental and calculated property data are now available. For more

06/20/2005 10783325.trn

information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10783325.str



chain nodes :

10 17 18 19 22

ring nodes :

1 2 3 4 5 6 7 8 9 11 12 13 14 15 16

chain bonds :

5-10 9-17 12-18 17-18 18-19

ring bonds :

1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 11-12 11-16 12-13 13-14 14-15
15-16

exact/norm bonds :

5-10 12-18 17-18

exact bonds :

5-6 5-9 6-7 8-9 9-17 18-19

normalized bonds :

1-2 1-7 2-3 3-4 4-8 7-8 11-12 11-16 12-13 13-14 14-15 15-16

isolated ring systems :

containing 1 : 11 :

G1:X,CH3,CN,NO2,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS

22:CLASS 23:CLASS

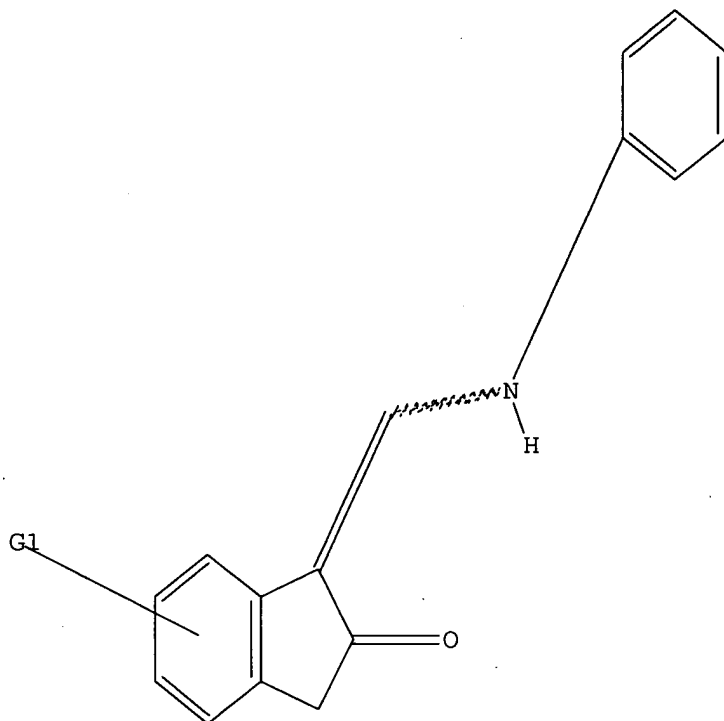
06/20/2005 10783325.trn

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 X, Me, CN, NO2, Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 11:39:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 119 TO ITERATE

100.0% PROCESSED 119 ITERATIONS
SEARCH TIME: 00.00.01

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1726 TO 3034
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 11:39:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2314 TO ITERATE

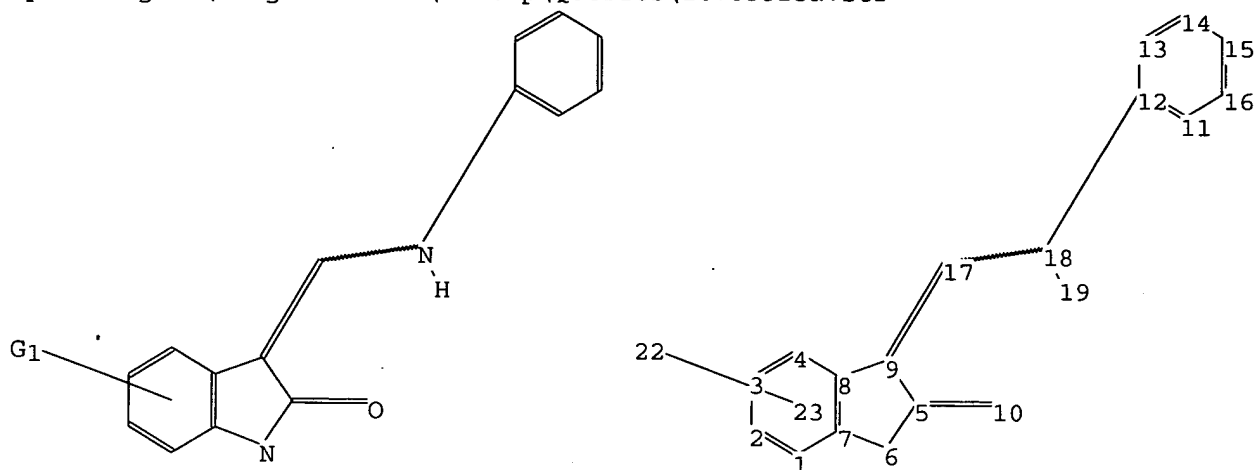
100.0% PROCESSED 2314 ITERATIONS
SEARCH TIME: 00.00.01

0 ANSWERS

L3 0 SEA SSS FUL L1

=>

Uploading C:\Program Files\Stnexp\Queries\10783325a.str



chain nodes :

10 17 18 19 22

ring nodes :

1 2 3 4 5 6 7 8 9 11 12 13 14 15 16

chain bonds :

5-10 9-17 12-18 17-18 18-19

ring bonds :

1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 11-12 11-16 12-13 13-14 14-15 15-16

exact/norm bonds :

5-6 5-10 6-7 12-18 17-18

exact bonds :

5-9 8-9 9-17 18-19

normalized bonds :

1-2 1-7 2-3 3-4 4-8 7-8 11-12 11-16 12-13 13-14 14-15 15-16

isolated ring systems :

containing 1 : 11 :

G1:X,CH3,CN,NO2,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS

22:CLASS 23:CLASS

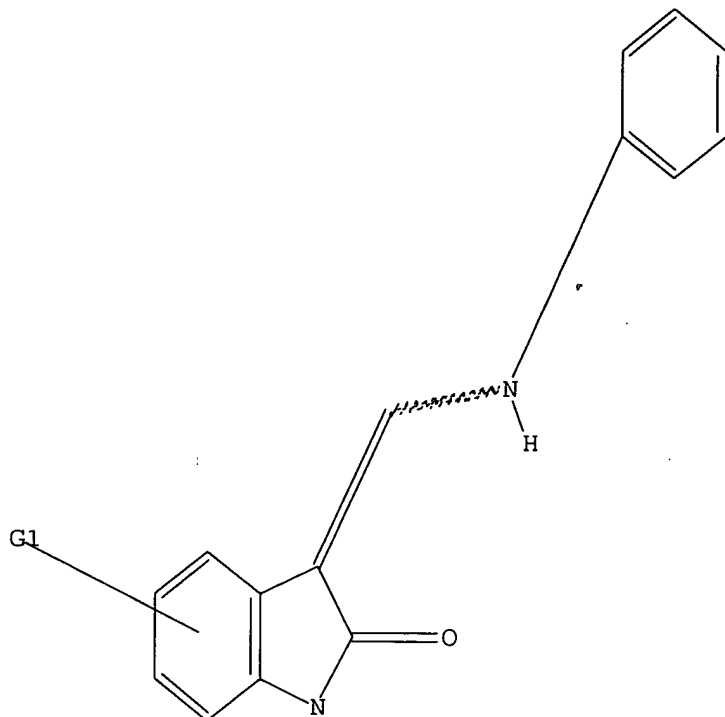
06/20/2005 10783325.trn

L4 STRUCTURE UPLOADED

=> d 14

L4 HAS NO ANSWERS

L4 STR



G1 X, Me, CN, NO2, Ak

Structure attributes must be viewed using STN Express query preparation.

=> s 14

SAMPLE SEARCH INITIATED 11:42:07 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 179 TO ITERATE

100.0% PROCESSED 179 ITERATIONS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

50 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 2778 TO 4382

PROJECTED ANSWERS: 1640 TO 2920

L5 50 SEA SSS SAM L4

=> s 14 sss full

FULL SEARCH INITIATED 11:42:14 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 3658 TO ITERATE

100.0% PROCESSED 3658 ITERATIONS

2057 ANSWERS

10783325.trn

Page 6

11:47

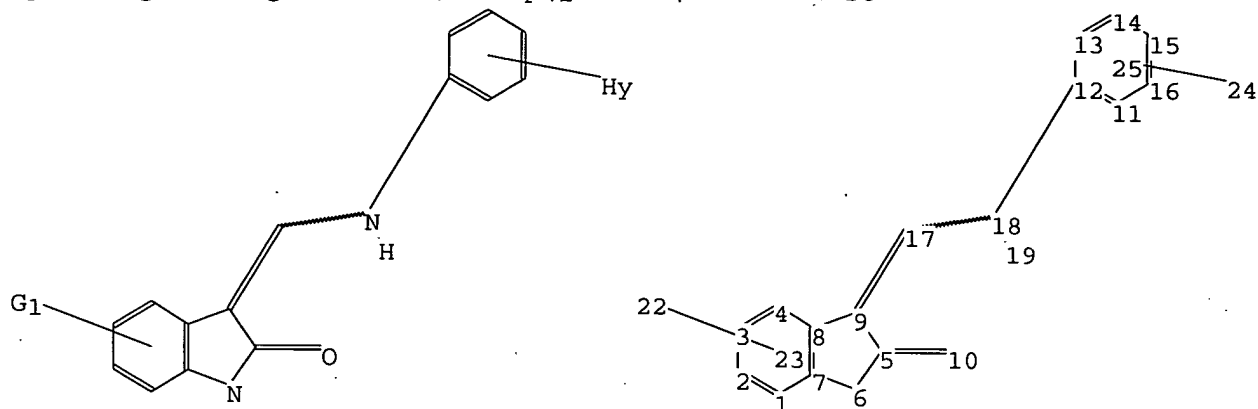
06/20/2005 10783325.trn

SEARCH TIME: 00.00.01

L6 2057 SEA SSS FUL L4

=>

Uploading C:\Program Files\Stnexp\Queries\10783325b.str



chain nodes :

10 17 18 19 22 24

ring nodes :

1 2 3 4 5 6 7 8 9 11 12 13 14 15 16

chain bonds :

5-10 9-17 12-18 17-18 18-19

ring bonds :

1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 11-12 11-16 12-13 13-14 14-15 15-16

exact/norm bonds :

5-6 5-10 6-7 12-18 17-18

exact bonds :

5-9 8-9 9-17 18-19

normalized bonds :

1-2 1-7 2-3 3-4 4-8 7-8 11-12 11-16 12-13 13-14 14-15 15-16

isolated ring systems :

containing 1 : 11 :

G1:X,CH3,CN,NO2,Ak

Match level :

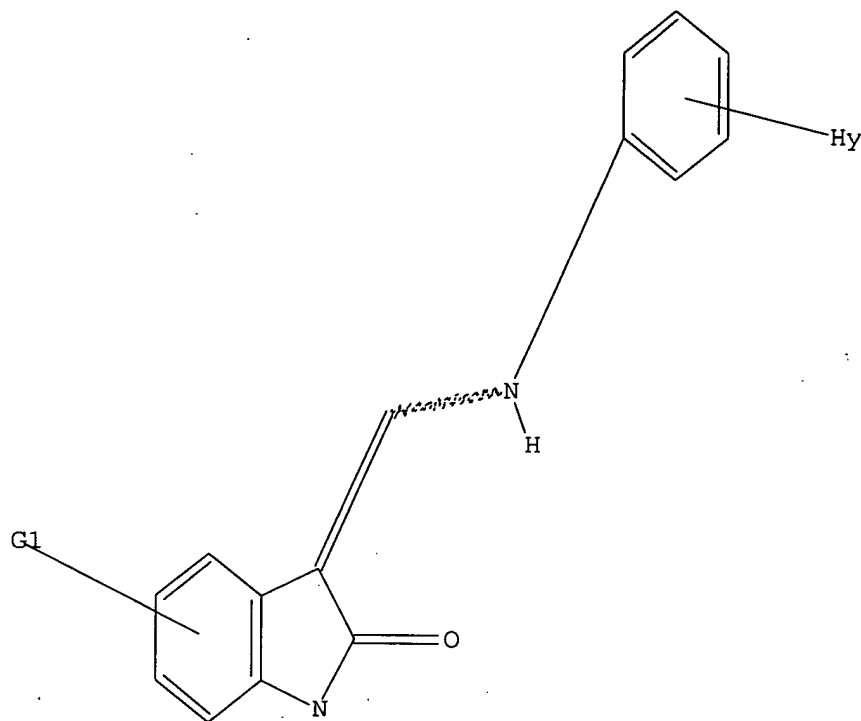
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11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
22:CLASS 23:CLASS 24:Atom 25:CLASS

L7 STRUCTURE UPLOADED

=> d 17

L7 HAS NO ANSWERS

L7 STR



G1 X, Me, CN, NO2, Ak

Structure attributes must be viewed using STN Express query preparation.

=> s 17

SAMPLE SEARCH INITIATED 11:44:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 177 TO ITERATE

100.0% PROCESSED 177 ITERATIONS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2742 TO 4338
PROJECTED ANSWERS: 5 TO 234

5 ANSWERS

L8 5 SEA SSS SAM L7

=> s 17 sss full

FULL SEARCH INITIATED 11:44:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 3609 TO ITERATE

100.0% PROCESSED 3609 ITERATIONS

82 ANSWERS

06/20/2005 10783325.trn

SEARCH TIME: 00.00.01

L9 82 SEA SSS FUL L7

=> FIL CAPLUS

COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
487.00	487.21

FILE 'CAPLUS' ENTERED AT 11:45:35 ON 20 JUN 2005
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FILE COVERS 1907 - 20 Jun 2005 VOL 142 ISS 26
FILE LAST UPDATED: 19 Jun 2005 (20050619/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 19

L10

14 L9

=> s 110 and py<=2001

21607156 PY<=2001

L11

7 L10 AND PY<=2001

=> d 110 ibib abs tot

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:965067 CAPLUS

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin
Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;
Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424
WO 2004096224	A3	20041216		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1473043	A1	20041103	EP 2003-9587	20030429
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: EP 2003-9587 A 20030429
EP 2004-508 A 20040113
EP 2004-1171 A 20040121

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination preps. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

L10 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:267298 CAPLUS

DOCUMENT NUMBER: 140:303523

TITLE: Preparation of heterocyclically substituted indolinones as inhibitors of various receptor tyrosine kinases

INVENTOR(S): Kley, Joerg; Heckel, Armin; Hilberg, Frank; Roth, Gerald Juergen; Lehmann-Lintz, Thorsten; Lotz, Ralf R. H.; Tontsch-Grunt, Ulrike; Van Meel, Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany

SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026829	A2	20040401	WO 2003-EP9978	20030909
WO 2004026829	A3	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
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DE 10242350 A1 20040318 DE 2002-10242350 20020912

DE 10252969 A1 20040527 DE 2002-10252969 20021114

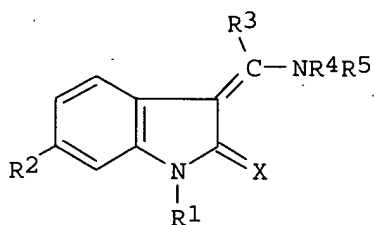
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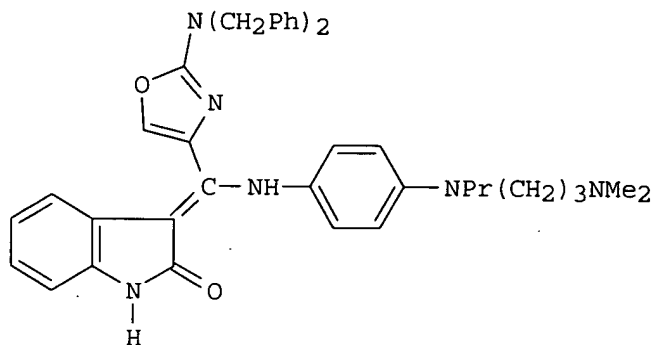
DE 2002-10252969 A 20021114

OTHER SOURCE(S): MARPAT 140:303523

GI



I



II

AB Title compds. I [X = O, S; R1 = H, prodrug residue, such as alkoxy carbonyl, acyl; R2 = H, F, Cl, Br, CN, NO2, (un)substituted CO2H, CONH2; R3 = (un)substituted 5-6-membered heteroaryl; R4 = (un)substituted cycloalkyl, aryl; R5 = H, alkyl] were prepared. I exhibit an inhibiting action on various receptor tyrosine kinases and cyclin-CDK complexes and on the proliferation of endothelial cells and various tumor cells. Thus, 1-acetyl-2-indolinone was treated with 2-dibenzylaminooxazole-4-carboxylic acid to give 1-acetyl-3-{1-hydroxy-1-[2-dibenzylaminooxazol-4-yl]methylene}-2-indolinone which was treated with Me2N(CH2)3NPrC6H4NH2-4 to give the title compound II which had IC50 for inhibition of cell proliferation of 1 nM.

L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:218460 CAPLUS

DOCUMENT NUMBER: 140:270851

TITLE: Preparation of heteroaryl-substituted
 aminomethylideneindolinones as cell proliferation

inhibitors.
 INVENTOR(S): Kley, Joerg; Heckel, Armin; Roth, Gerald Juergen;
 Lehmann-Lintz, Thorsten; Lotz, Ralf; Hilberg, Frank;
 Tontsch-Grunt, Ulrike; Van Meel, Jacobus
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.,
 Germany
 SOURCE: Ger. Offen., 114 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

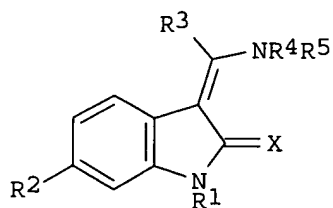
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10242350	A1	20040318	DE 2002-10242350	20020912
US 2005054710	A1	20050310	US 2003-656863	20030905
WO 2004026829	A2	20040401	WO 2003-EP9978	20030909
WO 2004026829	A3	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
 LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DE 2002-10242350	A	20020912
US 2002-414938P	P	20020930
DE 2002-10252969	A	20021114
US 2002-430790P	P	20021204

OTHER SOURCE(S): MARPAT 140:270851
 GI



I

AB Title compds. [I; X = O, S; R1 = H, alkoxycarbonyl, alkanoyl, other
 prodrug residue; R2 = H, F, Cl, Br, cyano, NO2, CO2H, alkoxycarbonyl,
 cycloalkoxycarbonyl, etc.; R3 = (Ph-condensed) 5-6 membered heteroaryl,
 etc.; R4 = (imino-interrupted) (substituted) cycloalkyl; R5 = H, alkyl],
 were prepared 1-Acetyl-3-[1-methoxy-1-(2-dibenzylamino-4-
 oxazolyl)methylene]-2-indolinone and N-propionyl-N-(3-dimethylaminopropyl)-
 p-phenylenediamine were heated in DMF at 120° for 3 h; the cooled
 mixture was treated with aqueous NaOH/MeOH followed by stirring for 1 h to give
 31% 3-(Z)-[1-[4-[N-propionyl-N-(3-dimethylaminopropyl)amino]phenylamino]-1-
 (2-dibenzylamino-4-oxazolyl)methylene]-2-indolinone. I inhibited HUVEC
 cell proliferation with IC50 = 0.2-120 nM.

L10 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:138723 CAPLUS
 DOCUMENT NUMBER: 140:193052
 TITLE: Use of LCK inhibitors for treatment of immunological diseases
 INVENTOR(S): Roth, Gerald Jurgen; Heckel, Armin; Walter, Rainer; Hilberg, Frank; Hauptmann, Rudolf; Ernst, Steffen; Stefanic, Martin; Colbatzky, Florian
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
 SOURCE: Ger. Offen., 12 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10237423	A1	20040219	DE 2002-10237423	20020816
CA 2495350	AA	20040304	CA 2003-2495350	20030811
WO 2004017948	A2	20040304	WO 2003-EP8890	20030811
WO 2004017948	A3	20040422		
WO 2004017948	C1	20050324		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1530466	A2	20050518	EP 2003-792292	20030811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004204458	A1	20041014	US 2003-640926	20030814
PRIORITY APPLN. INFO.:				
			DE 2002-10237423	A 20020816
			US 2002-409204P	P 20020909
			WO 2003-EP8890	W 20030811

AB The invention discloses a method for treatment of immunol. diseases or pathol. conditions which contain an immunol. component, using certain LCK inhibitors, which already are known as kinase inhibitors for therapy in oncol., optionally in combination with one or more other medications selected from NSAIDs, steroids, DMARDs, immunosuppressants, biol. response modifiers, and antiinfectives. Also disclosed are pharmaceutical compns. which contain the LCK inhibitors as well as the other medications, and use of LCK inhibitors for production of a pharmaceutical composition for treatment of immunol. diseases or pathol. conditions which contain an immunol. component.

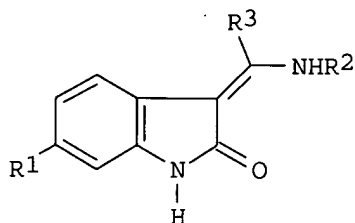
L10 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80649 CAPLUS
 DOCUMENT NUMBER: 140:146001
 TITLE: Preparation of indoline derivatives substituted in position 6 as antitumor agents
 INVENTOR(S): Roth, Gerald Juergen; Heckel, Armin; Kley, Joerg; Lehmann-Lintz, Thorsten; Hilberg, Frank;

PATENT ASSIGNEE(S): Tontsch-Grunt, Ulrike; Van Meel, Jacobus C. A.
 SOURCE: Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany
 PCT Int. Appl., 162 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009547	A1	20040129	WO 2003-EP7961	20030722
W: AE, AG, AL, AM, AT , AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10233366	A1	20040212	DE 2002-10233366	20020723
DE 10328533	A1	20050217	DE 2003-10328533	20030624
CA 2493436	AA	20040129	CA 2003-2493436	20030722
US 2005043389	A1	20050224	US 2003-625101	20030722
EP 1523473	A1	20050420	EP 2003-765079	20030722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012799	A	20050503	BR 2003-12799	20030722
PRIORITY APPLN. INFO.:				
			DE 2002-10233366	A 20020723
			US 2002-403106P	P 20020813
			DE 2003-10328533	A 20030624
			WO 2003-EP7961	W 20030722

OTHER SOURCE(S): MARPAT 140:146001
 GI



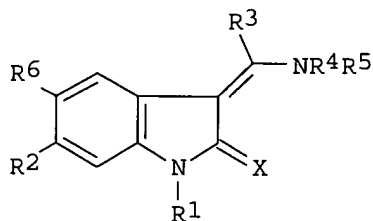
I

AB Indolines I [R1 = F, Cl, Br, CN; R2, R3 = (un)substituted Ph], the tautomers, enantiomers thereof, the mixts. and salts thereof, were prepared for use as inhibitors of various receptor tyrosine kinases and of the proliferation of endothelial cells and various tumor cells (no data). Thus, 2,5-F2C6H3NO2 was treated with CH2(CO2Me)2, decarboxylated and cyclized to 6-fluoro-2-indolinone which was N-acetylated and treated with 3-IC6H4CO2H to give 1-acetyl-3-[1-hydroxy-1-(3-iodophenyl)methylene]-6-chloro-2-indolinone. The latter compound was O-methylated and treated with

MeSO₂NMeC₆H₄NH₂-4 to give I [R₁ = Cl, R₂ = C₆H₄NMeSO₂Me-4, R₂ = C₆H₄I-3].
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2004:80648 CAPLUS
 DOCUMENT NUMBER: 140:146000
 TITLE: Preparation of indoline derivatives substituted in
 position 6 as antitumor agents
 INVENTOR(S): Roth, Gerald Juergen; Heckel, Armin; Kley, Joerg;
~~Seimann-Lintz~~; Thorsten; Hilberg, Frank;
 Tontsch-Grunt; Ulrike; Van Meel, Jacobus
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany
 SOURCE: PCT Int. Appl., 355 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009546	A1	20040129	WO 2003-EP7960	20030722
W: AE, AG, AL, AM, AT , AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10233366	A1	20040212	DE 2002-10233366	20020723
CA 2493721	AA	20040129	CA 2003-2493721	20030722
EP 1527046	A1	20050504	EP 2003-765078	20030722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			DE 2002-10233366	A 20020723
			WO 2003-EP7960	W 20030722
OTHER SOURCE(S):			MARPAT 140:146000	
GI				



AB Indolines I [X = O, S; R₁ = H, alkoxycarbonyl, acyl, (un)substituted
 CH₂NH₂; R₂ = F, Cl, Br, CN; R₃ = (un)substituted Ph, naphthyl; R₄ =

benzopyrazolyl, (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl; R6 = H, NO2], the tautomers, enantiomers, diastereomers thereof, the mixts. and salts thereof, were prepared for use as inhibitors of various receptor tyrosine kinases and of the proliferation of endothelial cells and various tumor cells (no data). Thus, 6-chloro-2-indolinone was N-acetylated and treated with PhC(OEt)₃ to give 1-acetyl-3-(1-ethoxy-1-phenylmethylene)-6-chloro-2-indolinone which was treated with Me₂NCH₂CH₂N(SO₂Me)C₆H₄NH₂-4 to give I [X = O, R1, R5, R6 = H, R2 = Cl, R3 = Ph, R4 = C₆H₄N(SO₂Me)CH₂CH₂NMe₂-4].

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:261836 CAPLUS

DOCUMENT NUMBER: 138:287525

TITLE: Preparation of 3-(arylamino)methylene-1,3-dihydro-2H-indol-2-ones as tyrosine kinase inhibitors for regulating, modulating and/or inhibiting abnormal cell proliferation

INVENTOR(S): Andrews, Steven W.; Wurster, Julie A.; Hull, Clarence III; Wang, Edward H.; Malone, Thomas

PATENT ASSIGNEE(S): Allergan, Inc., USA

SOURCE: PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

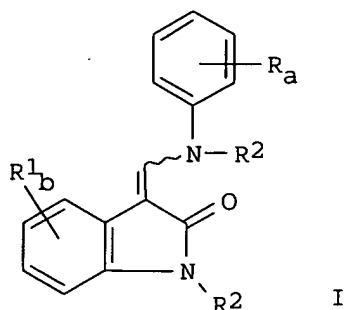
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003027102	A1	20030403	WO 2002-US30882	20020927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2461812	AA	20030403	CA 2002-2461812	20020927
US 2003199478	A1	20031023	US 2002-256879	20020927
US 6765012	B2	20040720		
US 2003225152	A1	20031204	US 2002-259703	20020927
EP 1430048	A1	20040623	EP 2002-776036	20020927
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508336	T2	20050331	JP 2003-530690	20020927
US 2004198720	A1	20041007	US 2004-783325	20040220
PRIORITY APPLN. INFO.:			US 2001-325815P	P 20010927
			US 2001-325819P	P 20010927
			US 2002-256879	A3 20020927
			WO 2002-US30882	W 20020927

OTHER SOURCE(S): MARPAT 138:287525

GI



AB The present invention relates to 3-(arylamino)methylene-1,3-dihydro-2H-indol-2-ones (shown as I; variables defined below; e.g. 3-[(4-morpholinophenylamino)methylene]-1,3-dihydroindol-2-one), capable of modulating tyrosine kinase signal transduction to regulate, modulate and/or inhibit abnormal cell proliferation. For I: R1 = halogen, NO₂, CN, C1-C4 alkyl and aryl; R2 = H, C1-C8 alkyl, COCH₃, CH₂CH₂OH, CH₂CH₂CH₂OH and phenyl; R = D, halogen, C1-C8 alkyl, CF₃, OCF₃, OCF₂H, CH₂CN, CN, SR₂, (CR₇R₈)cC(O)OR₂, C(O)N(R₂)₂, (CR₇R₈)cOR₂, HNC(O)R₂, HNC(O)OR₂, (CR₇R₈)cN(R₂)₂, SO₂(CR₇R₈)cN(R₂)₂, OP(O)(OR₂)₂, OC(O)OR₂, OCH₂O, HNCH:CH, -N(COR₂)CH₂CH₂, HC:NNH, N:CHS, O(CR₇R₈)dR₆, (CR₇R₈)cR₆ and NR₂(CR₇R₈)dR₆. B = 0-3; a = 0-5; c = 0-4; d = 2-5; the wavy line = a E or Z bond; addnl. definitions are given in the claims. Inhibitory biol. data are presented for ≤323 examples of I for the following assays: VEGF stimulated calcium ion signal in vitro, KDR, VEGF-induced dermal extravasation in guinea pig (Miles Assay), and laser-induced choroidal neovascularization in rat. Although the methods of preparation are not claimed, .apprx.80 example preps. are included.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:283925 CAPLUS

DOCUMENT NUMBER: 134:311105

TITLE: Preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation

INVENTOR(S): Heckel, Armin; Roth, Gerald Juergen; Walter, Rainer; Van Meel, Jacobus; Redemann, Norbert; Tontsch-Grunt, Ulrike; Spevak, Walter; Hilberg, Frank

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 282 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027081	A1	20010419	WO 2000-EP9867	20001009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,				

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19949208	A1	20010419	DE 1999-19949208	19991013
DE 10042696	A1	20020314	DE 2000-10042696	20000831
US 6762180	B1	20040713	US 2000-678682	20001003
CA 2387013	AA	20010419	CA 2000-2387013	20001009
BR 2000014735	A	20020716	BR 2000-14735	20001009
EP 1224170	A1	20020724	EP 2000-971347	20001009

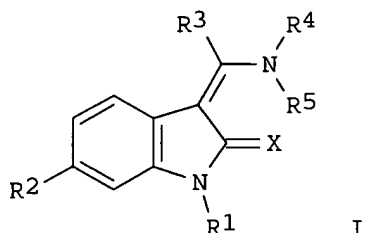
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003511441	T2	20030325	JP 2001-530102	20001009
EE 200200197	A	20030616	EE 2002-197	20001009
NZ 518489	A	20050527	NZ 2000-518489	20001009
BG 106587	A	20030131	BG 2002-106587	20020405
ZA 2002002764	A	20040421	ZA 2002-2764	20020409
NO 2002001719	A	20020411	NO 2002-1719	20020411

PRIORITY APPLN. INFO.:

DE 1999-19949208	A	19991013
DE 2000-10042696	A	20000831
US 1999-160547P	P	19991020
WO 2000-EP9867	W	20001009

OTHER SOURCE(S): MARPAT 134:311105
GI



I

AB The invention relates to the preparation of substituted (Z)-aminomethyleneindolines I [wherein X = O or S; R1 = H, C1-4 alkoxy carbonyl, C2-4 alkanoyl; R2 = HO2C, C1-6 alkoxy carbonyl, C4-7 cycloalkoxy carbonyl, aryloxy carbonyl, aminocarbonyl, or alkyl-substituted aminocarbonyl; R3 = H, C1-6 alkyl, C3-7 cycloalkyl, CF3, heteroaryl, or (un)substituted Ph or naphthyl; R4 and R5 = independently C3-7 cycloalkyl, monosubstituted phenyl] isomers and salts thereof as receptor tyrosine kinase and cyclin/CDK complex inhibitors for the treatment of endothelial cells and tumor cell proliferation. For example, 1-acetyl-6-ethoxycarbonyl-3-(ethoxyphenylmethylene)-2-indolinone and N-(4-aminophenyl)-N-(3-dimethylaminopropyl)acetamide were stirred together in DMF at 100° for 3h followed by addition of piperidine to give I (X = O; R1 = H; R2 = EtO2C; R3 = EtO; R4 = (Me2NCH2CH2CH2)N(Ac)C6H4; R5 = H). I inhibited the proliferation of endothelial cells with an IC50 of 0.003 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 14 CAPLUS COPYRIGHT. 2005 ACS on STN
ACCESSION NUMBER: 2000:688216 CAPLUS
DOCUMENT NUMBER: 133:266726

TITLE: Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors

INVENTOR(S): Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 189.pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

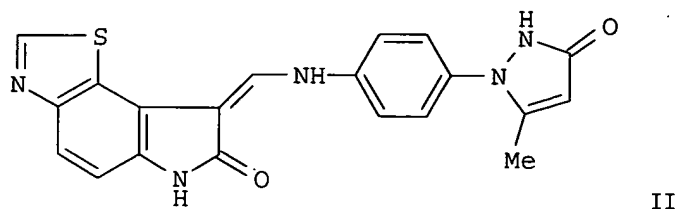
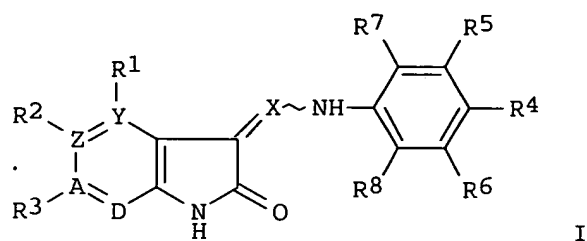
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056710	A1	20000928	WO 2000-US5057	20000228
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165514	A1	20020102	EP 2000-913643	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6350747	B1	20020226	US 2000-514528	20000228
JP 2002540097	T2	20021126	JP 2000-606572	20000228
US 6498176	B1	20021224	US 2001-914063	20010822
US 2002099071	A1	20020725	US 2001-966318	20010927
US 6818632	B2	20041116		
US 2004191210	A1	20040930	US 2003-742435	20031219
PRIORITY APPLN. INFO.:			GB 1999-4933	A 19990304
			US 2000-514528	A3 20000228
			WO 2000-US5057	W 20000228
			US 2001-966318	A3 20010927

OTHER SOURCE(S): MARPAT 133:266726

GI



AB The title compds. (I) [wherein X = N, CH, CCF₃, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R₁ = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH₂, CONH₂, or SO₂NH₂, alkoxy carbonyl, halo, CN, or NO₂; R₂ = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxy carbonyl), heterocyclyl, (un)substituted CONH₂, NH₂, or SO₂NH₂, halo, OH, NO₂, aliphatic sulfonyl, etc.; or R₁ and R₂ are joined to form an (un)substituted fused heterocyclic ring; R₃ = H, aliphatic, hydroxy(aliphatic), (un)substituted NH₂, CONH₂, or SO₂NH₂, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclloxy, or halo; or R₂ and R₃ are joined to form an (un)substituted fused heterocyclic ring; R₄ = SO₃H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO₂NH₂, NH₂, CONH₂, etc.; R₅ = H; or R₄ and R₅ are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2 (VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC₅₀ values of 1-10 μM and 11-50 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2000:227630 CAPLUS
 DOCUMENT NUMBER: 132:265083
 TITLE: Preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors
 INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin;

PATENT ASSIGNEE(S): Himmelsbach, Frank; Eberlein, Wolfgang; Roth, Gerald;
 SOURCE: Van Meel, Jacobus C. A.; Redemann, Norbert; Spevak,
 Walter; Tontsch-Grunt, Ulrike; Von Ruden, Thomas
 Boehringer Ingelheim Pharma K.-G., Germany
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19844003	A1	20000330	DE 1998-19844003	19980925
DE 19937496	A1	20010215	DE 1999-19937496	19990807
CA 2342622	AA	20000406	CA 1999-2342622	19990922
AU 9960863	A1	20000417	AU 1999-60863	19990922
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922
EP 1115704	B1	20030618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922
BG 105327	A	20011231	BG 2001-105327	20010309
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		
PRIORITY APPLN. INFO.:			DE 1998-19844003	A 19980925
			DE 1999-19937496	A 19990807
			WO 1999-EP7040	W 19990922
			US 2001-787974	B1 20011003
OTHER SOURCE(S):			MARPAT 132:265083	
GI				



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

PATENT INFORMATION:

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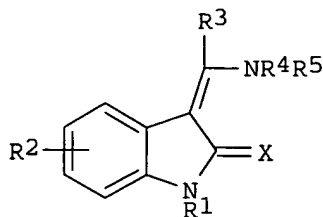
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NZ 510845	A	20031031	NZ 1999-510845	19990922
PT 1115704	T	20031128	PT 1999-947404	19990922
ES 2196860	T3	20031216	ES 1999-947404	19990922
BG 105327	A	20011231	BG 2001-105327	20010309
ZA 2001002260	A	20040419	ZA 2001-2260	20010319
HR 2001000216	A1	20020430	HR 2001-216	20010321
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US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:251076

GI



AB Title compds. [I; X = O, S; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, NO2; R3 = (substituted) Ph, naphthyl; R4 = H, alkyl; R5 = (substituted) Ph, naphthyl], were prepared. Thus, (Z)-3-[1-(4-piperidinomethylphenylamino)-1-phenylmethylidene]-5-nitro-2-indolinone [prepared from 3-(1-ethoxy-1-phenylmethylidene)-5-nitro-2-indolinone and 4-piperidinomethylaniline in DMF] inhibited proliferation of SCUT 1B tumor proliferation in mice with IC50 = 0.22 µM.

L10 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:784079 CAPLUS
 DOCUMENT NUMBER: 132:12258
 TITLE: Aminomethyleneindolinones with antitumor activity
 INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Norbert
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 112 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962882	A1	19991209	WO 1999-EP3692	19990528
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,				

MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
 TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19824922	A1	19991209	DE 1998-19824922	19980604
CA 2328291	AA	19991209	CA 1999-2328291	19990528
AU 9943707	A1	19991220	AU 1999-43707	19990528
AU 764782	B2	20030828		
BR 9910898	A	20010213	BR 1999-10898	19990528
EP 1100779	A1	20010523	EP 1999-926454	19990528

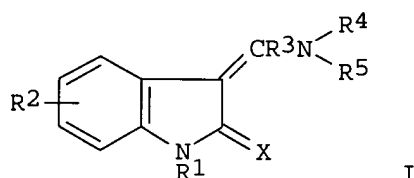
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 IE, SI, LT, LV, FI, RO

TR 200003515	T2	20010621	TR 2000-200003515	19990528
EE 200000723	A	20020415	EE 2000-723	19990528
JP 2002516906	T2	20020611	JP 2000-552094	19990528
US 6319918	B1	20011120	US 1999-323499	19990601
ZA 2000005435	A	20020107	ZA 2000-5435	20001005
BG 104938	A	20010629	BG 2000-104938	20001113
NO 2000006138	A	20010201	NO 2000-6138	20001201
HR 2000000831	A1	20011231	HR 2000-831	20001201
US 6545035	B1	20030408	US 2001-969912	20011003

PRIORITY APPLN. INFO.:

DE 1998-19824922	A	19980604
US 1998-92014P	P	19980708
WO 1999-EP3692	W	19990528
US 1999-323499	A3	19990601

OTHER SOURCE(S): MARPAT 132:12258
 GI



AB Title compds. I [X = O, S; R1 = H, alkoxy carbonyl, alkanoyl; R2 = CO2H, alkoxy carbonyl, (un)substituted CONH2; R3 = H, (un)substituted alkyl; R4 = H, (un)substituted alkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl] were prepared. Thus, 2-oxo-5-indolinecarboxylic acid was attached to Rink resin and treated with tri-Me ortho valerate to give polymer-bound 3-Z-(1-methoxy-1-butylmethylene)-2-oxo-5-indolinecarboxamide which was treated with 4-piperidinomethylaniline to give I [X = O, R1 = 5-CONH2, R2, R4 = H, R3 = Bu, R5 = 4-piperidinomethylanilino]. This compound had an IC50 for inhibition of SKUT-1B cell proliferation of 0.036 μ M.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:672749 CAPLUS

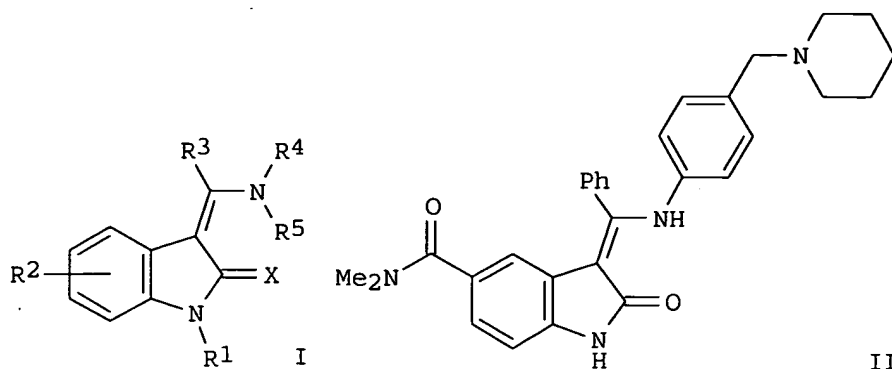
DOCUMENT NUMBER: 131:299364

TITLE: Substituted indolinones having an inhibiting effect on kinases and cyclin/CDK complexes

INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 101 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952869	A1	19991021	WO 1999-EP2436	19990410
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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DE 19816624	A1	19991021	DE 1998-19816624	19980415
US 6169106	B1	20010102	US 1999-286983	19990406
CA 2323111	AA	19991021	CA 1999-2323111	19990410
AU 9938149	A1	19991101	AU 1999-38149	19990410
AU 749829	B2	20020704		
BR 9909688	A	20001219	BR 1999-9688	19990410
EP 1071665	A1	20010131	EP 1999-920635	19990410
EP 1071665	B1	20031001		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002980	T2	20010221	TR 2000-200002980	19990410
EE 200000598	A	20020415	EE 2000-598	19990410
EE 4432	B1	20050215		
JP 2002511449	T2	20020416	JP 2000-543432	19990410
NZ 507967	A	20030429	NZ 1999-507967	19990410
AT 251138	E	20031015	AT 1999-920635	19990410
SK 283824	B6	20040203	SK 2000-1513	19990410
PT 1071665	T	20040227	PT 1999-920635	19990410
ES 2207209	T3	20040516	ES 1999-920635	19990410
TW 510897	B	20021121	TW 1999-88105963	19990414
ZA 2000004623	A	20010307	ZA 2000-4623	20000904
BG 104813	A	20010831	BG 2000-104813	20000929
BG 64443	B1	20050228		
NO 2000005151	A	20001013	NO 2000-5151	20001013
PRIORITY APPLN. INFO.:			DE 1998-19816624	A 19980415
			US 1998-90227P	P 19980622
			WO 1999-EP2436	W 19990410
OTHER SOURCE(S):	MARPAT 131:299364			
GI				



AB The invention relates to substituted indolinones I [X = O or S; R1 = H, alkoxy carbonyl, alkanoyl; R2 = CO2H, alkoxy carbonyl, or (di)alkylaminocarbonyl; R3 = (un)substituted Ph or naphthyl; R4 = H, alkyl; R5 = H, (un)substituted alkyl, cycloalkyl, indanyl, Ph, heteroaryl, pyrrolidinyl, or piperidinyl], their isomers, and their salts, especially their physiologically compatible salts. The compounds have valuable pharmacological properties, especially an inhibitory effect on various kinases and cyclin/CDK complexes, and on the proliferation of various tumor cells. The invention also relates to medicaments containing the compounds, to their use, and to methods for producing them. Approx. 160 example compounds and 7 pharmaceutical formulations are described. For instance, title compound II was prepared from 2-indolinone-5-carboxylic acid Me ester in 5 steps: (1) N-acetylation (86%); (2) condensation with PhC(OEt)₃ to give the 3-(1-ethoxy-1-phenylmethylene) derivative (67%); (3) condensation of the alkoxyethylene compound with a corresponding amine and deacetylation; (4) saponification of the Me ester; and (5) amidation of the resulting acid with dimethylamine (88%). In an assay against SK-UT-1B lung tumor cells in mice, II had an IC₅₀ value of 0.01 μM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:659664 CAPLUS

DOCUMENT NUMBER: 131:271809

TITLE: Preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as Cyclin dependent kinase inhibitors

INVENTOR(S): Grell, Wolfgang; Walter, Rainer; Heckel, Armin; Himmelsbach, Frank; Wittneben, Helmut; van Meel, Jakobus; Redemann, Norbert; Haigh, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 64 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

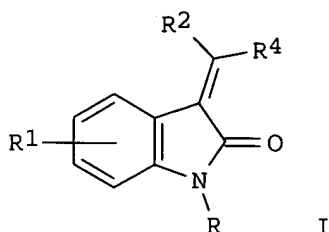
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19815020	A1	19991007	DE 1998-19815020	19980403
US 6043254	A	20000328	US 1999-277063	19990326
WO 9951590	A1	19991014	WO 1999-EP2186	19990330

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JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937034 A1 19991025 AU 1999-37034 19990330
PRIORITY APPLN. INFO.: DE 1998-19815020 A 19980403
US 1998-86733P P 19980526
WO 1999-EP2186 W 19990330

OTHER SOURCE(S): MARPAT 131:271809
GI



AB Title compds. [I; R = H; R1 = H, halo, NO2, (alkanoyl)amino, etc.; R2 = (un)substituted Ph; R4 = NHR3; R3 = heteroannelated Ph, heteroarylalk(en)ylphenyl, etc.] were prepared Thus, 2-indolinone was N-acetylated and the product condensed with PhC(OEt)3 to give I (R1 = H, R2 = Ph) (II; R = Ac, R4 = OEt) which was condensed with 5-aminoindole to give II (R = H, R4 = 5-indolylamino). Data for biol. activity of I were given.

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L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:283925 CAPLUS

DOCUMENT NUMBER: 134:311105

TITLE: Preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation

INVENTOR(S): Heckel, Armin; Roth, Gerald Juergen; Walter, Rainer; Van Meel, Jacobus; Redemann, Norbert; Tontsch-Grunt, Ulrike; Spevak, Walter; Hilberg, Frank

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 282 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

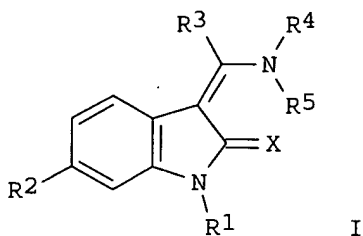
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001027081	A1	20010419	WO 2000-EP9867	20001009 <--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19949208	A1	20010419	DE 1999-19949208	19991013 <--
DE 10042696	A1	20020314	DE 2000-10042696	20000831
US 6762180	B1	20040713	US 2000-678682	20001003
CA 2387013	AA	20010419	CA 2000-2387013	20001009 <--
BR 2000014735	A	20020716	BR 2000-14735	20001009
EP 1224170	A1	20020724	EP 2000-971347	20001009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511441	T2	20030325	JP 2001-530102	20001009
EE 200200197	A	20030616	EE 2002-197	20001009
NZ 518489	A	20050527	NZ 2000-518489	20001009
BG 106587	A	20030131	BG 2002-106587	20020405
ZA 2002002764	A	20040421	ZA 2002-2764	20020409
NO 2002001719	A	20020411	NO 2002-1719	20020411
PRIORITY APPLN. INFO.:			DE 1999-19949208	A 19991013
			DE 2000-10042696	A 20000831
			US 1999-160547P	P 19991020
			WO 2000-EP9867	W 20001009

OTHER SOURCE(S): MARPAT 134:311105
GI



AB The invention relates to the preparation of substituted (Z)-aminomethyleneindolines I [wherein X = O or S; R1 = H, C1-4 alkoxy carbonyl, C2-4 alkanoyl; R2 = HO2C, C1-6 alkoxy carbonyl, C4-7 cycloalkoxy carbonyl, aryloxy carbonyl, aminocarbonyl, or alkyl-substituted aminocarbonyl; R3 = H, C1-6 alkyl, C3-7 cycloalkyl, CF3, heteroaryl, or (un)substituted Ph or naphthyl; R4 and R5 = independently C3-7 cycloalkyl, monosubstituted phenyl] isomers and salts thereof as receptor tyrosine kinase and cyclin/CDK complex inhibitors for the treatment of endothelial cells and tumor cell proliferation. For example, 1-acetyl-6-ethoxycarbonyl-3-(ethoxyphenylmethylene)-2-indolinone and N-(4-aminophenyl)-N-(3-dimethylaminopropyl)acetamide were stirred together in DMF at 100° for 3h followed by addition of piperidine to give I (X = O; R1 = H; R2 = EtO2C; R3 = EtO; R4 = (Me2NCH2CH2CH2)N(Ac)C6H4; R5 = H). I inhibited the proliferation of endothelial cells with an IC50 of 0.003 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:688216 CAPLUS

DOCUMENT NUMBER: 133:266726

TITLE: Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors

INVENTOR(S): Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 189 pp.

CODEN: PIXXD2

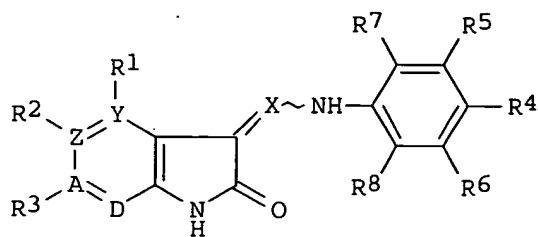
DOCUMENT TYPE: Patent

LANGUAGE: English

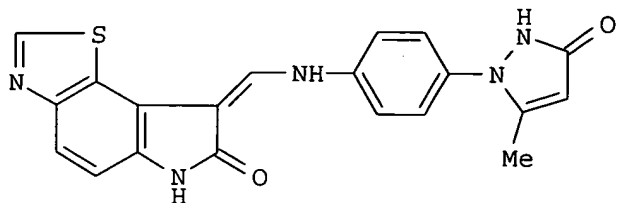
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056710	A1	20000928	WO 2000-US5057	20000228 <--
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165514	A1	20020102	EP 2000-913643	20000228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6350747	B1	20020226	US 2000-514528	20000228
JP 2002540097	T2	20021126	JP 2000-606572	20000228
US 6498176	B1	20021224	US 2001-914063	20010822
US 2002099071	A1	20020725	US 2001-966318	20010927
US 6818632	B2	20041116		
US 2004191210	A1	20040930	US 2003-742435	20031219
PRIORITY APPLN. INFO.:			GB 1999-4933	A 19990304
			US 2000-514528	A3 20000228
			WO 2000-US5057	W 20000228
			US 2001-966318	A3 20010927
OTHER SOURCE(S):	MARPAT 133:266726			
GI				



I



II

AB The title compds. (I) [wherein X = N, CH, CCF₃, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R₁ = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH₂, CONH₂, or SO₂NH₂, alkoxycarbonyl, halo, CN, or NO₂; R₂ = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxy carbonyl), heterocyclyl, (un)substituted CONH₂, NH₂, or SO₂NH₂, halo, OH, NO₂, aliphatic sulfonyl, etc.; or R₁ and R₂ are joined to form an (un)substituted fused heterocyclic ring; R₃ = H, aliphatic, hydroxy(aliphatic), (un)substituted NH₂, CONH₂, or SO₂NH₂, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocyclloxy, or halo; or R₂ and R₃ are joined to form an (un)substituted fused heterocyclic ring; R₄ = SO₃H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO₂NH₂, NH₂, CONH₂, etc.; R₅ = H; or R₄ and R₅ are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2 (VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC₅₀ values of 1-10 μM and 11-50 μM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:227630 CAPLUS

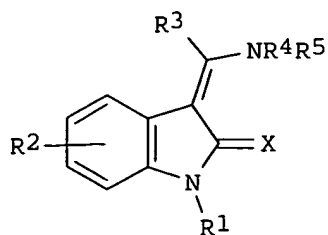
DOCUMENT NUMBER: 132:265083

TITLE: Preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors

INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin;

PATENT ASSIGNEE(S): Himmelsbach, Frank; Eberlein, Wolfgang; Roth, Gerald;
 SOURCE: Van Meel, Jacobus C. A.; Redemann, Norbert; Spevak,
 Walter; Tontsch-Grunt, Ulrike; Von Ruden, Thomas
 Boehringer Ingelheim Pharma K.-G., Germany
 PCT Int. Appl., 269 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
DE 19937496	A1	20010215	DE 1999-19937496	19990807 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
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JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922
BG 105327	A	20011231	BG 2001-105327	20010309 <--
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322 <--
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		
PRIORITY APPLN. INFO.:			DE 1998-19844003	A 19980925
			DE 1999-19937496	A 19990807
			WO 1999-EP7040	W 19990922
			US 2001-787974	B1 20011003
OTHER SOURCE(S):			MARPAT 132:265083	
GI				



AB Title compds. [I; R1 = H, OH, alkyl; R2 = H, halo, NO2, alkyl; R3 = (un)substituted Ph or -naphthyl; R4 = H or alkyl; R5 = (un)substituted alkylphenyl or -alkylnaphthyl; X = O or S] were prepared. Thus, 2-indolinone was N-acetyltated and the product condensed with PhC(OEt)₃ to give, after PhNH₂ treatment, I (R1 = R2 = R4 = H, R3 = R5 = Ph, X = O). Data for biol. activity of I were given.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:206644 CAPLUS

DOCUMENT NUMBER: 132:251076

TITLE: Preparation of aminoarylmethylideneindolinones as kinase inhibitors.

INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Van Meel, Jakobus; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Rueden, Thomas
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: Ger. Offen., 66 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
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TR 200100854	T2	20011221	TR 2001-200100854	19990922 <--

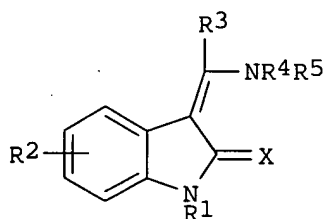
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922
PT 1115704	T	20031128	PT 1999-947404	19990922
ES 2196860	T3	20031216	ES 1999-947404	19990922
BG 105327	A	20011231	BG 2001-105327	20010309 <--
ZA 2001002260	A	20040419	ZA 2001-2260	20010319
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322 <--
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:251076

GI



AB Title compds. [I; X = O, S; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, NO2; R3 = (substituted) Ph, naphthyl; R4 = H, alkyl; R5 = (substituted) Ph, naphthyl], were prepared. Thus, (Z)-3-[1-(4-piperidinomethylphenylamino)-1-phenylmethylidene]-5-nitro-2-indolinone [prepared from 3-(1-ethoxy-1-phenylmethylidene)-5-nitro-2-indolinone and 4-piperidinomethylaniline in DMF] inhibited proliferation of SCUT 1B tumor proliferation in mice with IC50 = 0.22 μ M.

L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:784079 CAPLUS

DOCUMENT NUMBER: 132:12258

TITLE: Aminomethyleneindolinones with antitumor activity

INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Norbert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

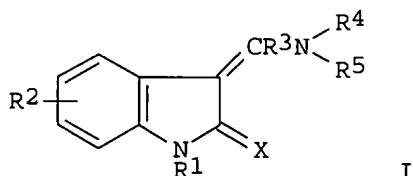
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962882	A1	19991209	WO 1999-EP3692	19990528 <--
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 TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19824922	A1	19991209	DE 1998-19824922	19980604 <--
CA 2328291	AA	19991209	CA 1999-2328291	19990528 <--
AU 9943707	A1	19991220	AU 1999-43707	19990528 <--
AU 764782	B2	20030828		
BR 9910898	A	20010213	BR 1999-10898	19990528 <--
EP 1100779	A1	20010523	EP 1999-926454	19990528 <--
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EE 200000723	A	20020415	EE 2000-723	19990528
JP 2002516906	T2	20020611	JP 2000-552094	19990528
US 6319918	B1	20011120	US 1999-323499	19990601 <--
ZA 2000005435	A	20020107	ZA 2000-5435	20001005
BG 104938	A	20010629	BG 2000-104938	20001113 <--
NO 2000006138	A	20010201	NO 2000-6138	20001201 <--
HR 2000000831	A1	20011231	HR 2000-831	20001201 <--
US 6545035	B1	20030408	US 2001-969912	20011003
PRIORITY APPLN. INFO.:			DE 1998-19824922	A 19980604
			US 1998-92014P	P 19980708
			WO 1999-EP3692	W 19990528
			US 1999-323499	A3 19990601

OTHER SOURCE(S): MARPAT 132:12258
 GI



AB Title compds. I [X = O, S; R1 = H, alkoxy-carbonyl, alkanoyl; R2 = CO2H, alkoxy-carbonyl, (un)substituted CONH2; R3 = H, (un)substituted alkyl; R4 = H, (un)substituted alkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl] were prepared. Thus, 2-oxo-5-indolinecarboxylic acid was attached to Rink resin and treated with tri-Me ortho-valerate to give polymer-bound 3-Z-(1-methoxy-1-butylmethylene)-2-oxo-5-indolinecarboxamide which was treated with 4-piperidinomethylaniline to give I [X = O, R1 = 5-CONH2, R2, R4 = H, R3 = Bu, R5 = 4-piperidinomethylanilino]. This compound had an IC50 for inhibition of SKUT-1B cell proliferation of 0.036 μ M.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:672749 CAPLUS

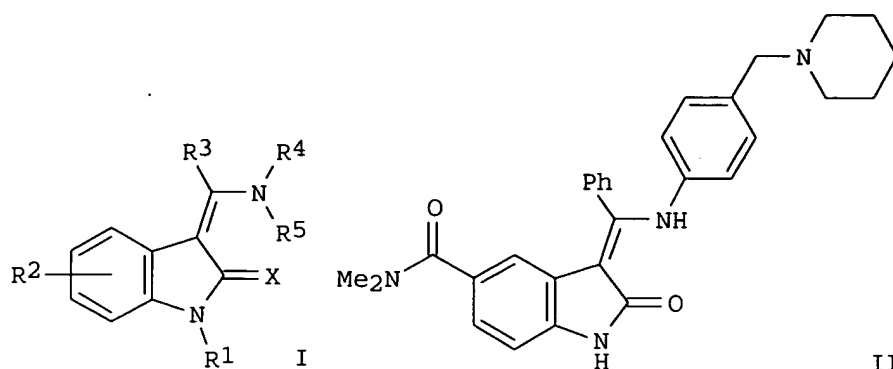
DOCUMENT NUMBER: 131:299364

TITLE: Substituted indolinones having an inhibiting effect on kinases and cyclin/CDK complexes

INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 101 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952869	A1	19991021	WO 1999-EP2436	19990410 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19816624	A1	19991021	DE 1998-19816624	19980415 <--
US 6169106	B1	20010102	US 1999-286983	19990406 <--
CA 2323111	AA	19991021	CA 1999-2323111	19990410 <--
AU 9938149	A1	19991101	AU 1999-38149	19990410 <--
AU 749829	B2	20020704		
BR 9909688	A	20001219	BR 1999-9688	19990410 <--
EP 1071665	A1	20010131	EP 1999-920635	19990410 <--
EP 1071665	B1	20031001		
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TR 200002980	T2	20010221	TR 2000-200002980	19990410 <--
EE 200000598	A	20020415	EE 2000-598	19990410
EE 4432	B1	20050215		
JP 2002511449	T2	20020416	JP 2000-543432	19990410
NZ 507967	A	20030429	NZ 1999-507967	19990410
AT 251138	E	20031015	AT 1999-920635	19990410
SK 283824	B6	20040203	SK 2000-1513	19990410
PT 1071665	T	20040227	PT 1999-920635	19990410
ES 2207209	T3	20040516	ES 1999-920635	19990410
TW 510897	B	20021121	TW 1999-88105963	19990414
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NO 2000005151	A	20001013	NO 2000-5151	20001013 <--
PRIORITY APPLN. INFO.:				
			DE 1998-19816624	A 19980415
			US 1998-90227P	P 19980622
			WO 1999-EP2436	W 19990410
OTHER SOURCE(S): MARPAT 131:299364				
GI				



AB The invention relates to substituted indolinones I [X = O or S; R1 = H, alkoxy carbonyl, alkanoyl; R2 = CO₂H, alkoxy carbonyl, or (di)alkylaminocarbonyl; R3 = (un)substituted Ph or naphthyl; R4 = H, alkyl; R5 = H, (un)substituted alkyl, cycloalkyl, indanyl, Ph, heteroaryl, pyrrolidinyl, or piperidinyl], their isomers, and their salts, especially their physiol. compatible salts. The compds. have valuable pharmacol. properties, especially an inhibitory effect on various kinases and cyclin/CDK complexes, and on the proliferation of various tumor cells. The invention also relates to medicaments containing the compds., to their use, and to methods for producing them. Approx. 160 example compds. and 7 pharmaceutical formulations are described. For instance, title compound II was prepared from 2-indolinone-5-carboxylic acid Me ester in 5 steps: (1) N-acetylation (86%); (2) condensation with PhC(OEt)₃ to give the 3-(1-ethoxy-1-phenylmethylene) derivative (67%); (3) condensation of the alkoxy methylene compound with a corresponding amine and deacetylation; (4) saponification of the Me ester; and (5) amidation of the resulting acid with dimethylamine (88%). In an assay against SK-UT-1B lung tumor cells in mice, II had an IC₅₀ value of 0.01 μM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:659664 CAPLUS

DOCUMENT NUMBER: 131:271809

TITLE: Preparation of 3-(α-heteroarylaminobenzylidene)-2-indolinones as Cyclin dependent kinase inhibitors

INVENTOR(S): Grell, Wolfgang; Walter, Rainer; Heckel, Armin; Himmelsbach, Frank; Wittneben, Helmut; van Meel, Jakobus; Redemann, Norbert; Haigh, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 64 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

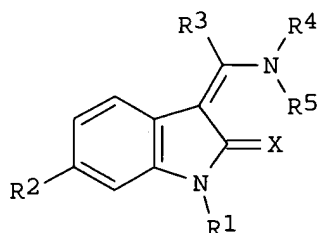
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19815020	A1	19991007	DE 1998-19815020	19980403 <--
US 6043254	A	20000328	US 1999-277063	19990326 <--
WO 9951590	A1	19991014	WO 1999-EP2186	19990330 <--

WO 2001027081	A1	20010419	WO 2000-EP9867	20001009 <--
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DE 10042696	A1	20020314	DE 2000-10042696	20000831
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CA 2387013	AA	20010419	CA 2000-2387013	20001009 <--
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EP 1224170	A1	20020724	EP 2000-971347	20001009
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JP 2003511441	T2	20030325	JP 2001-530102	20001009
EE 200200197	A	20030616	EE 2002-197	20001009
NZ 518489	A	20050527	NZ 2000-518489	20001009
BG 106587	A	20030131	BG 2002-106587	20020405
ZA 2002002764	A	20040421	ZA 2002-2764	20020409
NO 2002001719	A	20020411	NO 2002-1719	20020411
PRIORITY APPLN. INFO.:			DE 1999-19949208	A 19991013
			DE 2000-10042696	A 20000831
			US 1999-160547P	P 19991020
			WO 2000-EP9867	W 20001009

OTHER SOURCE(S): MARPAT 134:311105
GI



I

AB The invention relates to the preparation of substituted (Z)-aminomethyleneindolines I [wherein X = O or S; R1 = H, C1-4 alkoxy carbonyl, C2-4 alkanoyl; R2 = HO2C, C1-6 alkoxy carbonyl, C4-7 cycloalkoxy carbonyl, aryloxy carbonyl, aminocarbonyl, or alkyl-substituted aminocarbonyl; R3 = H, C1-6 alkyl, C3-7 cycloalkyl, CF3, heteroaryl, or (un)substituted Ph or naphthyl; R4 and R5 = independently C3-7 cycloalkyl, monosubstituted phenyl] isomers and salts thereof as receptor tyrosine kinase and cyclin/CDK complex inhibitors for the treatment of endothelial cells and tumor cell proliferation. For example, 1-acetyl-6-ethoxycarbonyl-3-(ethoxyphenylmethylene)-2-indolinone and N-(4-aminophenyl)-N-(3-dimethylaminopropyl)acetamide were stirred together in DMF at 100° for 3h followed by addition of piperidine to give I (X = O; R1 = H; R2 = EtO2C; R3 = EtO; R4 = (Me2NCH2CH2CH2)N(Ac)C6H4; R5 = H). I inhibited the proliferation of endothelial cells with an IC50 of 0.003 μM.

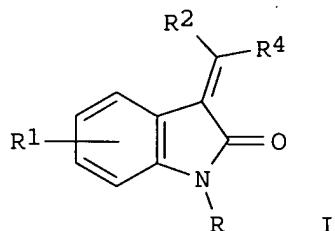
IT 334949-31-4P

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MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM

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ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9937034 A1 19991025 AU 1999-37034 19990330 <--
PRIORITY APPLN. INFO.: DE 1998-19815020 A 19980403
US 1998-86733P P 19980526
WO 1999-EP2186 W 19990330

OTHER SOURCE(S): MARPAT 131:271809
GI



AB Title compds. [I; R = H; R1 = H, halo, NO2, (alkanoyl)amino, etc.; R2 = (un)substituted Ph; R4 = NHR3; R3 = heteroannelated Ph, heteroarylalk(en)ylphenyl, etc.] were prepared Thus, 2-indolinone was N-acetylated and the product condensed with PhC(OEt)3 to give I (R1 = H, R2 = Ph) (II; R = Ac, R4 = OEt) which was condensed with 5-aminoindole to give II (R = H, R4 = 5-indolylamino). Data for biol. activity of I were given.

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:283925 CAPLUS

DOCUMENT NUMBER: 134:311105

TITLE: Preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation

INVENTOR(S): Heckel, Armin; Roth, Gerald Juergen; Walter, Rainer; Van Meel, Jacobus; Redemann, Norbert; Tontsch-Grunt, Ulrike; Spevak, Walter; Hilberg, Frank

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 282 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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06/20/2005

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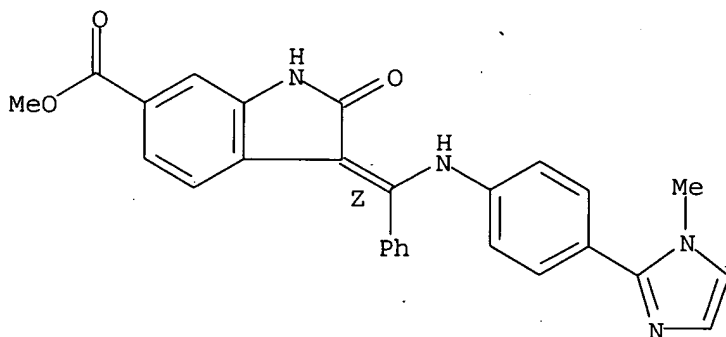
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(title compds.; preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation)

RN 334949-31-4 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 334949-72-3P 334950-27-5P 334950-34-4P

334950-35-5P 334951-02-9P 334951-03-0P

334951-04-1P 334951-11-0P 334951-73-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(title compds.; preparation of substituted aminomethyleneindolinone inhibitors of tyrosine receptor kinases and CDK/cyclin kinases as antitumor agents and inhibitors of cell proliferation)

RN 334949-72-3 CAPLUS

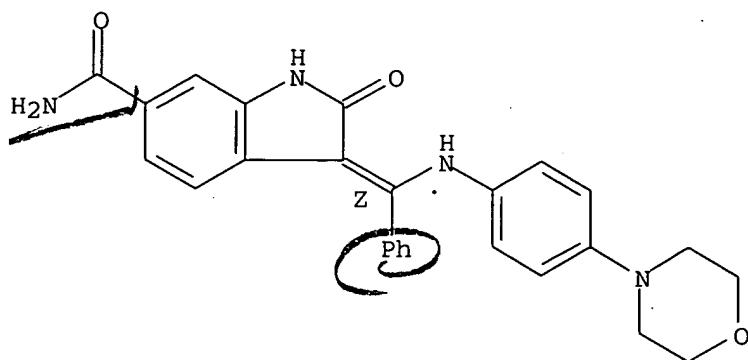
CN 1H-Indole-6-carboxamide, 2,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 334949-71-2

CMF C26 H24 N4 O3

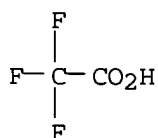
Double bond geometry as shown.



CM 2

CRN 76-05-1

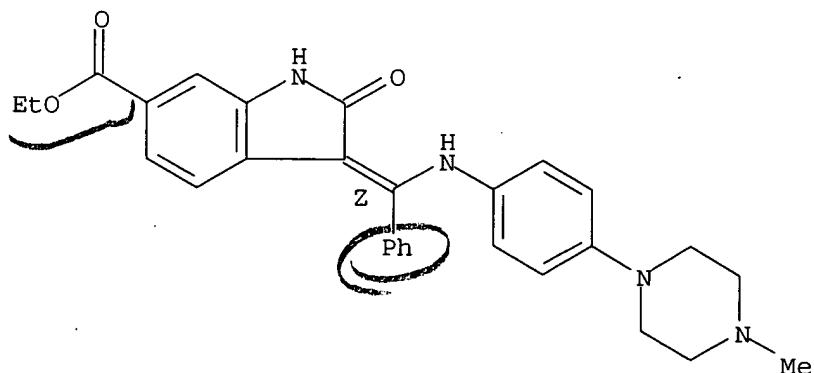
CMF C2 H F3 O2



RN 334950-27-5 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(4-methyl-1-piperazinyl)phenyl]amino]phenylmethylene]-2-oxo-, ethyl ester, (3Z)- (9CI)
(CA INDEX NAME)

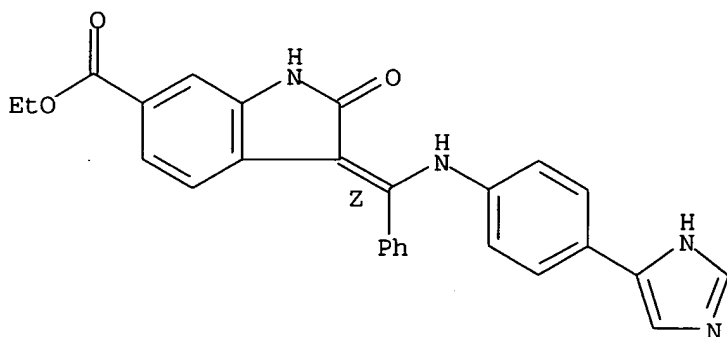
Double bond geometry as shown.



RN 334950-34-4 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-2-oxo-, ethyl ester, (3Z)- (9CI) (CA INDEX NAME)

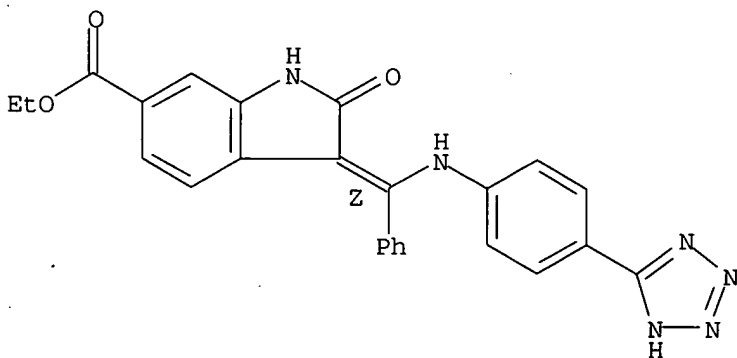
Double bond geometry as shown.



RN 334950-35-5 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[phenyl[[4-(1H-tetrazol-5-yl)phenyl]amino]methylene]-, ethyl ester, (3Z)- (9CI) (CA INDEX NAME)

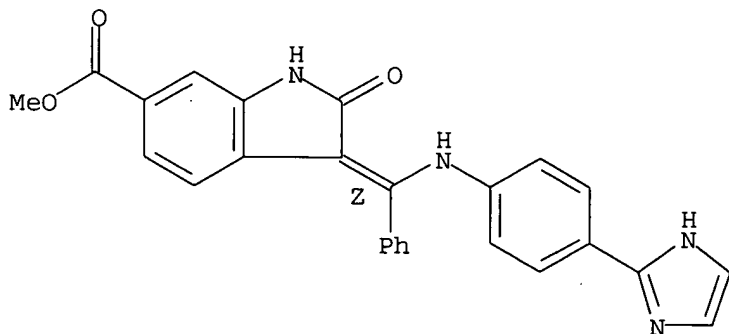
Double bond geometry as shown.



RN 334951-02-9 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

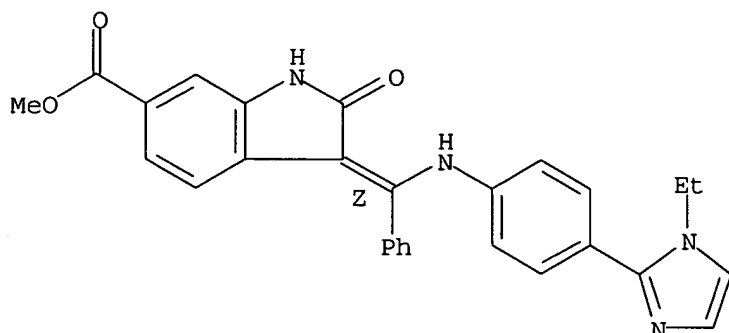


RN 334951-03-0 CAPLUS

CN 1H-Indole-6-carboxylic acid, 3-[[[4-(1-ethyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2,3-dihydro-2-oxo-, methyl ester, (3Z)-

(9CI) (CA INDEX NAME)

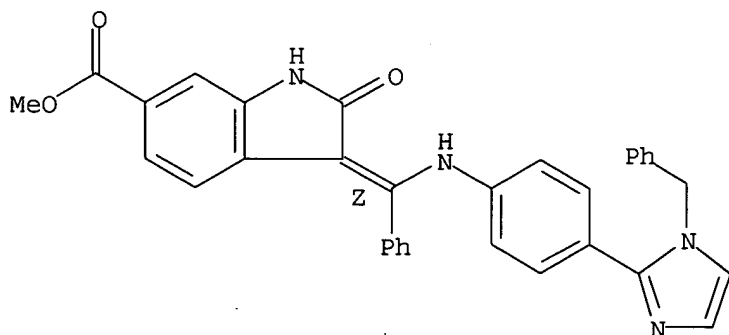
Double bond geometry as shown.



RN 334951-04-1 CAPLUS

CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-2-oxo-3-[phenyl[[4-[1-(phenylmethyl)-1H-imidazol-2-yl]phenyl]amino]methylene]-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

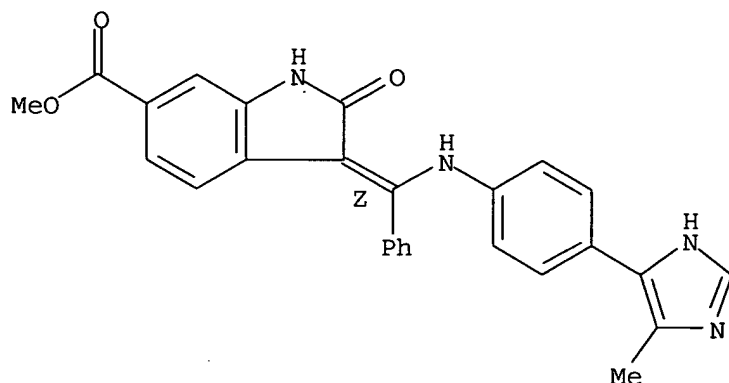
Double bond geometry as shown.



RN 334951-11-0 CAPLUS

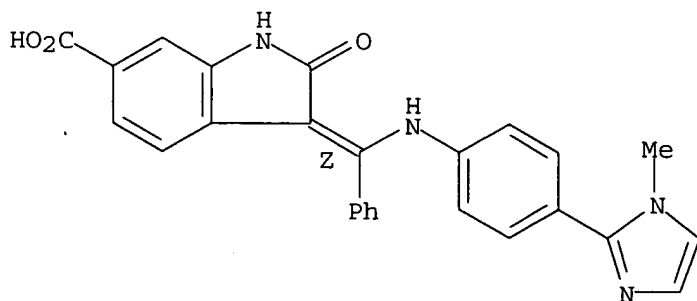
CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(5-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-2-oxo-, methyl ester, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 334951-73-4 CAPLUS
 CN 1H-Indole-6-carboxylic acid, 2,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2000:688216 CAPLUS
 DOCUMENT NUMBER: 133:266726
 TITLE: Preparation of 3-(anilinomethylene)oxindoles and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors
 INVENTOR(S): Glennon, Kimberley Caroline; Kuyper, Lee Frederick; Lackey, Karen Elizabeth; McNutt, Robert Walton, Jr.
 PATENT ASSIGNEE(S): Glaxo Group Limited, UK
 SOURCE: PCT Int. Appl., 189 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056710	A1	20000928	WO 2000-US5057	20000228 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1165514 A1 20020102 EP 2000-913643 20000228

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

US 6350747 B1 20020226 US 2000-514528 20000228

JP 2002540097 T2 20021126 JP 2000-606572 20000228

US 6498176 B1 20021224 US 2001-914063 20010822

US 2002099071 A1 20020725 US 2001-966318 20010927

US 6818632 B2 20041116

US 2004191210 A1 20040930 US 2003-742435 20031219

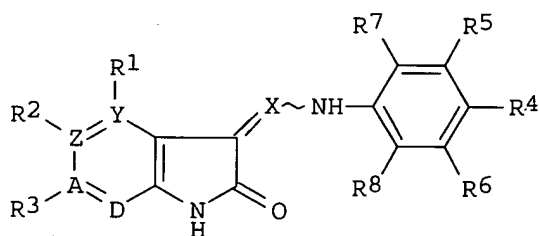
PRIORITY APPLN. INFO.: GB 1999-4933 A 19990304

US 2000-514528 A3 20000228

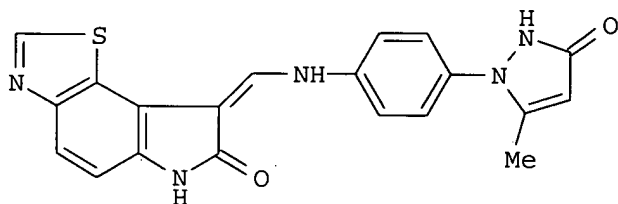
WO 2000-US5057 W 20000228

US 2001-966318 A3 20010927

OTHER SOURCE(S): MARPAT 133:266726
GI



I



II

AB The title compds. (I) [wherein X = N, CH, CCF₃, or C(aliphatic); Y, Z, A, and D = C or N, and the number of N ≤ 1; R₁ = H, aliphatic, SH, hydroxy(aliphatic), aryl(aliphatic), cycloalkyl(aliphatic), heterocyclyl(aliphatic), (un)substituted NH₂, CONH₂, or SO₂NH₂, alkoxy(alkyl), halo, CN, or NO₂; R₂ = H, aliphatic, hydroxyimino aliphatic, alkoxy(carbonyl), hydroxyaliph., aryl(oxycarbonyl), heterocyclyl, (un)substituted CONH₂, NH₂, or SO₂NH₂, halo, OH, NO₂, aliphatic sulfonyl, etc.; or R₁ and R₂ are joined to form an (un)substituted fused heterocyclic ring; R₃ = H, aliphatic, hydroxy(aliphatic), (un)substituted NH₂, CONH₂, or SO₂NH₂, alkoxy, aryl(oxy), hydroxyaryl, (hydroxy)heterocyclyl, heterocycliloxy, or halo; or R₂ and R₃ are joined to form an (un)substituted fused heterocyclic ring; R₄ = SO₃H, (aliphatic)sulfonyl(aliphatic), (un)substituted SO₂NH₂, NH₂, CONH₂, etc.; R₅ = H; or R₄ and R₅ are joined to form an (un)substituted fused heterocyclic ring] were prepared via standard synthetic methods and solution phase library techniques as vascular endothelial growth factor receptor type 2

(VEGFR-2), cyclin dependent kinase 2 (CDK2), tyrosine kinase Tie-2 receptor, and colony-stimulating factor 1 receptor kinase (c-fms) inhibitors. For example, a mixture of 8-dimethylaminomethylene-6,8-dihydro-1-thia-3,6-diaza-as-indacene-7-one (preparation given) and 2-(4-aminophenyl)-3-methylpyrazolin-5-one in absolute EtOH was heated with stirring at 90°C for 16 h to give (Z)-II (83%). In substrate phosphorylation assays, II inhibited VEGFR-2 and CDK2 with IC50 values of 1-10 µM and 11-50 µM, resp. I are useful as therapeutic agents in disease states alleviated by the inhibition or antagonism of protein kinase activated signalling pathways in general, and in particular in the pathol. processes which involve aberrant cellular proliferation, such as tumor growth, restenosis, atherosclerosis, and thrombosis. I are particularly useful for suppressing tumor growth by inhibiting tumor-related angiogenesis.

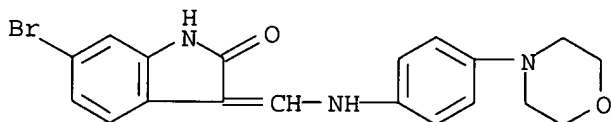
IT 297754-04-2P 297754-40-6P, 3-[[4-(4-Morpholinyl)anilino]methylidene]-6-vinyl-1,3-dihydro-2H-indol-2-one
297754-49-5P, 6-Bromo-3-[[4-(5-methyl-3-oxo-2,3-dihydro-1H-pyrazol-1-yl)anilino]methylidene]-1,3-dihydro-2H-indol-2-one 297756-72-0P
, 3-[(Z)-[4-(4-Morpholinyl)anilino]methylidene]-6-vinyl-1,3-dihydro-2H-indol-2-one

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of anilinomethylene oxindolones and analogs as protein tyrosine kinase and protein serine/threonine kinase inhibitors by alkylation and amination of oxindolones via standard or solution phase library methods)

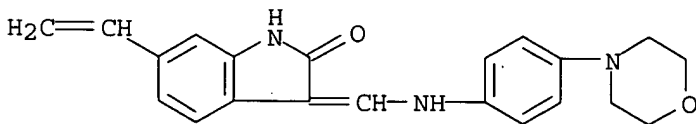
RN 297754-04-2 CAPLUS

CN 2H-Indol-2-one, 6-bromo-1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]methylene]- (9CI) (CA INDEX NAME)



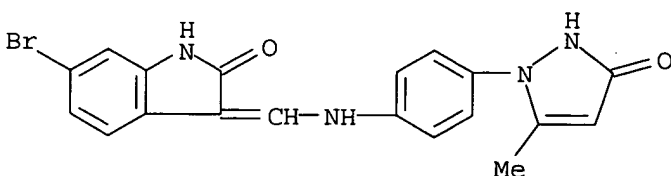
RN 297754-40-6 CAPLUS

CN 2H-Indol-2-one, 6-ethenyl-1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]methylene]- (9CI) (CA INDEX NAME)



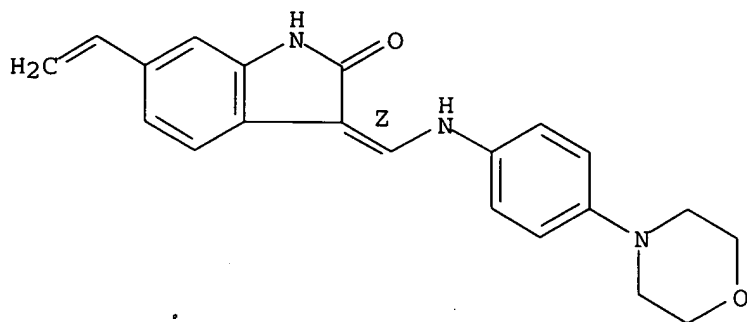
RN 297754-49-5 CAPLUS

CN 2H-Indol-2-one, 6-bromo-3-[[[4-(2,3-dihydro-5-methyl-3-oxo-1H-pyrazol-1-yl)phenyl]amino]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 297756-72-0 CAPLUS
 CN 2H-Indol-2-one, 6-ethenyl-1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2000:227630 CAPLUS
 DOCUMENT NUMBER: 132:265083
 TITLE: Preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors
 INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Roth, Gerald; Van Meel, Jacobus C. A.; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Ruden, Thomas
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 269 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
DE 19937496	A1	20010215	DE 1999-19937496	19990807 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
EP 1115704	B1	20030618		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

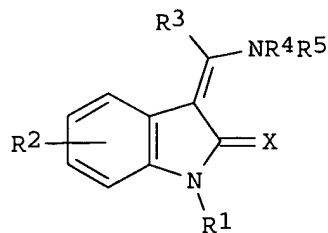
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922
BG 105327	A	20011231	BG 2001-105327	20010309 <--
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322 <--
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:265083

GI



I

AB Title compds. [I; R1 = H, OH, alkyl; R2 = H, halo, NO2, alkyl; R3 = (un)substituted Ph or -naphthyl; R4 = H or alkyl; R5 = (un)substituted alkylphenyl or -alkylnaphthyl; X = O or S] were prepared. Thus, 2-indolinone was N-acetyltated and the product condensed with PhC(OEt)3 to give, after PhNH2 treatment, I (R1 = R2 = R4 = H, R3 = R5 = Ph, X = O). Data for biol. activity of I were given.

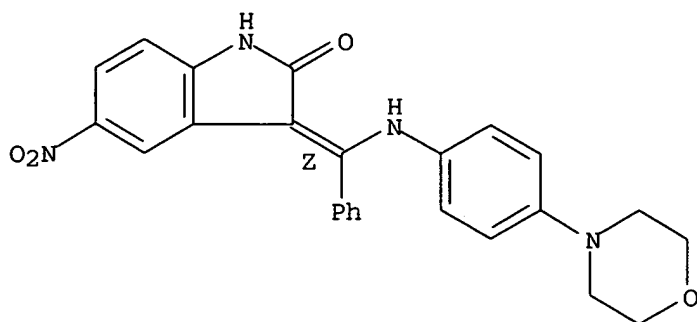
IT **262366-61-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-aminobenzylideneindolinones as cyclin dependent kinase inhibitors)

RN 262366-61-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:206644 CAPLUS

DOCUMENT NUMBER: 132:251076

TITLE: Preparation of aminoarylmethylideneindolinones as kinase inhibitors.

INVENTOR(S): Walter, Rainer; Grell, Wolfgang; Heckel, Armin; Himmelsbach, Frank; Eberlein, Wolfgang; Van Meel, Jakobus; Redemann, Norbert; Spevak, Walter; Tontsch-Grunt, Ulrike; Von Rueden, Thomas

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 66 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

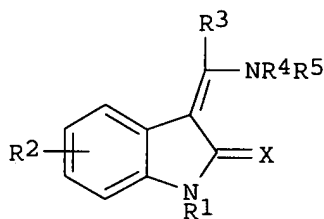
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19844003	A1	20000330	DE 1998-19844003	19980925 <--
CA 2342622	AA	20000406	CA 1999-2342622	19990922 <--
WO 2000018734	A1	20000406	WO 1999-EP7040	19990922 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960863	A1	20000417	AU 1999-60863	19990922 <--
AU 763361	B2	20030717		
EP 1115704	A1	20010718	EP 1999-947404	19990922 <--
EP 1115704	B1	20030618		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100854	T2	20011221	TR 2001-200100854	19990922 <--
JP 2002525356	T2	20020813	JP 2000-572194	19990922
EE 200100184	A	20020815	EE 2001-184	19990922
AT 243195	E	20030715	AT 1999-947404	19990922
NZ 510845	A	20031031	NZ 1999-510845	19990922

PT 1115704	T	20031128	PT 1999-947404	19990922
ES 2196860	T3	20031216	ES 1999-947404	19990922
BG 105327	A	20011231	BG 2001-105327	20010309 <--
ZA 2001002260	A	20040419	ZA 2001-2260	20010319
HR 2001000216	A1	20020430	HR 2001-216	20010321
NO 2001001477	A	20010322	NO 2001-1477	20010322 <--
US 2004058978	A1	20040325	US 2003-666643	20030919
US 6855710	B2	20050215		

PRIORITY APPLN. INFO.:

DE 1998-19844003	A	19980925
DE 1999-19937496	A	19990807
WO 1999-EP7040	W	19990922
US 2001-787974	B1	20011003

OTHER SOURCE(S): MARPAT 132:251076
GI

AB Title compds. [I; X = O, S; R1 = H, alkyl; R2 = H, F, Cl, Br, iodo, alkyl, NO2; R3 = (substituted) Ph, naphthyl; R4 = H, alkyl; R5 = (substituted) Ph, naphthyl], were prepared. Thus, (Z)-3-[1-(4-piperidinomethylphenylamino)-1-phenylmethylidene]-5-nitro-2-indolinone [prepared from 3-(1-ethoxy-1-phenylmethylidene)-5-nitro-2-indolinone and 4-piperidinomethylaniline in DMF] inhibited proliferation of SCUT 1B tumor proliferation in mice with IC50 = 0.22 μ M.

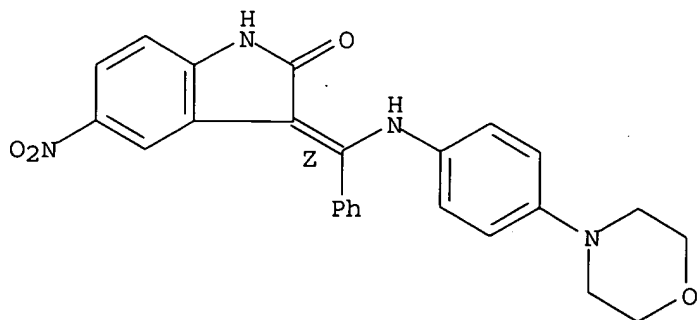
IT 262366-61-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoarylmethylideneindolinones as kinase inhibitors)

RN 262366-61-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

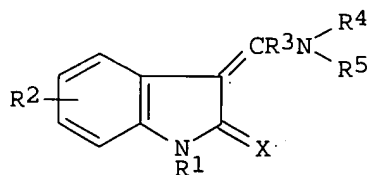
Double bond geometry as shown.



L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:784079 CAPLUS
 DOCUMENT NUMBER: 132:12258
 TITLE: Aminomethyleneindolinones with antitumor activity
 INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Norbert
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: PCT Int. Appl., 112 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962882	A1	19991209	WO 1999-EP3692	19990528 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19824922	A1	19991209	DE 1998-19824922	19980604 <--
CA 2328291	AA	19991209	CA 1999-2328291	19990528 <--
AU 9943707	A1	19991220	AU 1999-43707	19990528 <--
AU 764782	B2	20030828		
BR 9910898	A	20010213	BR 1999-10898	19990528 <--
EP 1100779	A1	20010523	EP 1999-926454	19990528 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200003515	T2	20010621	TR 2000-200003515	19990528 <--
EE 200000723	A	20020415	EE 2000-723	19990528
JP 2002516906	T2	20020611	JP 2000-552094	19990528
US 6319918	B1	20011120	US 1999-323499	19990601 <--
ZA 2000005435	A	20020107	ZA 2000-5435	20001005
BG 104938	A	20010629	BG 2000-104938	20001113 <--
NO 2000006138	A	20010201	NO 2000-6138	20001201 <--
HR 2000000831	A1	20011231	HR 2000-831	20001201 <--
US 6545035	B1	20030408	US 2001-969912	20011003
PRIORITY APPLN. INFO.:				
			DE 1998-19824922	A 19980604
			US 1998-92014P	P 19980708
			WO 1999-EP3692	W 19990528
			US 1999-323499	A3 19990601
OTHER SOURCE(S): MARPAT 132:12258				
GI				



I

AB Title compds. I [X = O, S; R1 = H, alkoxycarbonyl, alkanoyl; R2 = CO2H, alkoxycarbonyl, (un)substituted CONH2; R3 = H, (un)substituted alkyl; R4 = H, (un)substituted alkyl, Ph, naphthyl, heteroaryl; R5 = H, alkyl] were prepared Thus, 2-oxo-5-indolinecarboxylic acid was attached to Rink resin and treated with tri-Me orthovalerate to give polymer-bound 3-Z-(1-methoxy-1-butylmethylene)-2-oxo-5-indolinecarboxamide which was treated with 4-piperidinomethylaniline to give I [X = O, R1 = 5-CONH2, R2, R4 = h, R3 = Bu, R5 = 4-piperidinomethylanilino]. This compound had an IC50 for inhibition of SKUT-1B cell proliferation of 0.036 μ M.

IT 251550-82-0P

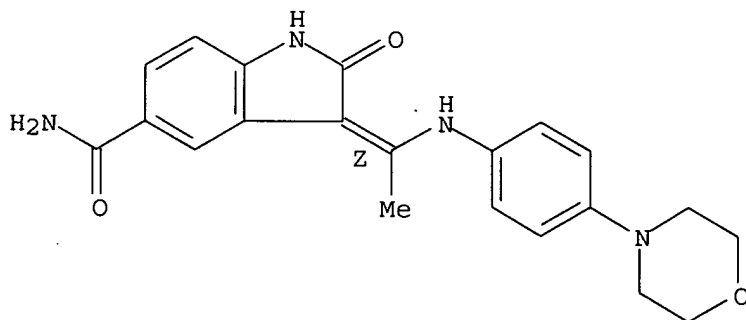
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminomethyleneindolinones with antitumor activity)

RN 251550-82-0 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[1-[[4-(4-morpholinyl)phenyl]amino]ethylidene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:672749 CAPLUS

DOCUMENT NUMBER: 131:299364

TITLE: Substituted indolinones having an inhibiting effect on kinases and cyclin/CDK complexes

INVENTOR(S): Heckel, Armin; Walter, Rainer; Grell, Wolfgang; Van Meel, Jacobus C. A.; Redemann, Robert

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952869	A1	19991021	WO 1999-EP2436	19990410 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,				

RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19816624	A1	19991021	DE 1998-19816624	19980415 <--
US 6169106	B1	20010102	US 1999-286983	19990406 <--
CA 2323111	AA	19991021	CA 1999-2323111	19990410 <--
AU 9938149	A1	19991101	AU 1999-38149	19990410 <--
AU 749829	B2	20020704		
BR 9909688	A	20001219	BR 1999-9688	19990410 <--
EP 1071665	A1	20010131	EP 1999-920635	19990410 <--
EP 1071665	B1	20031001		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

TR 200002980	T2	20010221	TR 2000-200002980	19990410 <--
EE 200000598	A	20020415	EE 2000-598	19990410
EE 4432	B1	20050215		
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NZ 507967	A	20030429	NZ 1999-507967	19990410
AT 251138	E	20031015	AT 1999-920635	19990410
SK 283824	B6	20040203	SK 2000-1513	19990410
PT 1071665	T	20040227	PT 1999-920635	19990410
ES 2207209	T3	20040516	ES 1999-920635	19990410
TW 510897	B	20021121	TW 1999-88105963	19990414
ZA 2000004623	A	20010307	ZA 2000-4623	20000904 <--
BG 104813	A	20010831	BG 2000-104813	20000929 <--
BG 64443	B1	20050228		
NO 2000005151	A	20001013	NO 2000-5151	20001013 <--

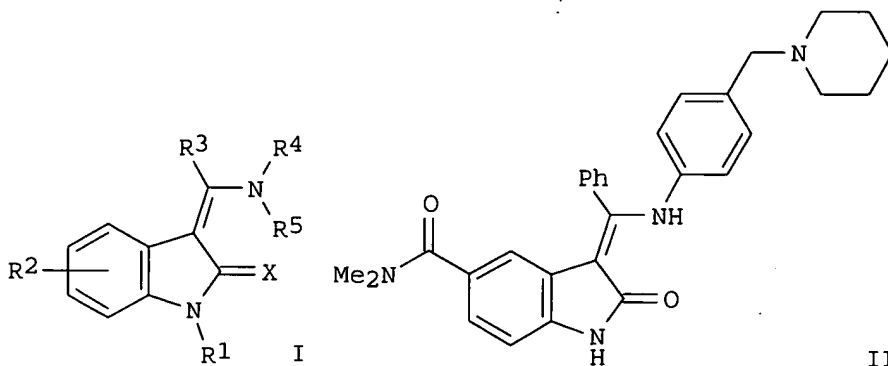
PRIORITY APPLN. INFO.:

DE 1998-19816624	A	19980415
US 1998-90227P	P	19980622
WO 1999-EP2436	W	19990410

OTHER SOURCE(S):

MARPAT 131:299364

GI



AB The invention relates to substituted indolinones I [X = O or S; R1 = H, alkoxy carbonyl, alkanoyl; R2 = CO2H, alkoxy carbonyl, or (di)(alkyl)aminocarbonyl; R3 = (un)substituted Ph or naphthyl; R4 = H, alkyl; R5 = H, (un)substituted alkyl, cycloalkyl, indanyl, Ph, heteroaryl, pyrrolidinyl, or piperidinyl], their isomers, and their salts, especially their physiologically compatible salts. The compounds have valuable pharmacological properties, especially an inhibitory effect on various kinases and cyclin/CDK complexes, and on the proliferation of various tumor cells. The invention

also relates to medicaments containing the compds., to their use, and to methods for producing them. Approx. 160 example compds. and 7 pharmaceutical formulations are described. For instance, title compound II was prepared from 2-indolinone-5-carboxylic acid Me ester in 5 steps: (1) N-acetylation (86%); (2) condensation with PhC(OEt)_3 to give the 3-(1-ethoxy-1-phenylmethylene) derivative (67%); (3) condensation of the alkoxymethylene compound with a corresponding amine and deacetylation; (4) saponification of the Me ester; and (5) amidation of the resulting acid with dimethylamine (88%). In an assay against SK-UT-1B lung tumor cells in mice, II had an IC_{50} value of $0.01 \mu\text{M}$.

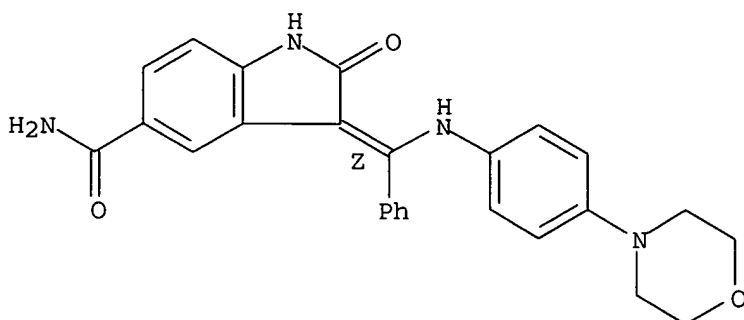
IT 247083-50-7P 247083-71-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of indolinones as inhibitors of kinases and cyclin/CDK complexes)

RN 247083-50-7 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[[[4-(4-morpholinyl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

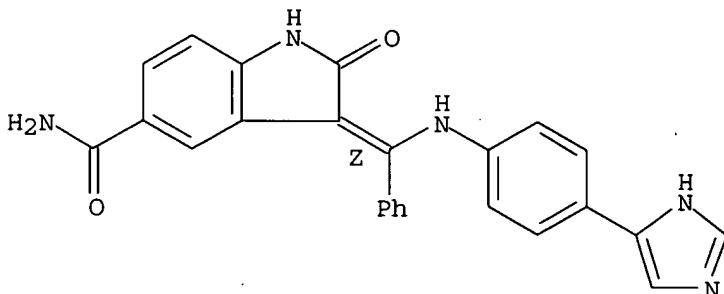
Double bond geometry as shown.



RN 247083-71-2 CAPLUS

CN 1H-Indole-5-carboxamide, 2,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-2-oxo-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

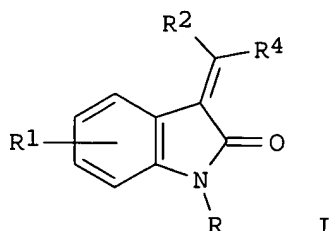


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659664 CAPLUS

DOCUMENT NUMBER: 131:271809
 TITLE: Preparation of 3-(α -heteroarylaminobenzylidene)-
 2-indolinones as Cyclin dependent kinase inhibitors
 INVENTOR(S): Grell, Wolfgang; Walter, Rainer; Heckel, Armin;
 Himmelsbach, Frank; Wittneben, Helmut; van Meel,
 Jakobus; Redemann, Norbert; Haigh, Robert
 PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
 SOURCE: Ger. Offen., 64 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19815020	A1	19991007	DE 1998-19815020	19980403 <--
US 6043254	A	20000328	US 1999-277063	19990326 <--
WO 9951590	A1	19991014	WO 1999-EP2186	19990330 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937034	A1	19991025	AU 1999-37034	19990330 <--
PRIORITY APPLN. INFO.:			DE 1998-19815020	A 19980403
			US 1998-86733P	P 19980526
			WO 1999-EP2186	W 19990330
OTHER SOURCE(S):			MARPAT 131:271809	
GI				



AB Title compds. [I; R = H; R1 = H, halo, NO2, (alkanoyl)amino, etc.; R2 = (un)substituted Ph; R4 = NHR3; R3 = heteroannelated Ph, heteroarylalk(en)ylphenyl, etc.] were prepared Thus, 2-indolinone was N-acetylated and the product condensed with PhC(OEt)3 to give I (R1 = H, R2 = Ph) (II; R = Ac, R4 = OEt) which was condensed with 5-aminoindole to give II (R = H, R4 = 5-indolylamino). Data for biol. activity of I were given.

IT 245545-75-9P 245545-89-5P 245545-90-8P
 245545-92-0P 245545-95-3P 245546-03-6P
 245546-07-0P 245546-19-4P 245546-20-7P

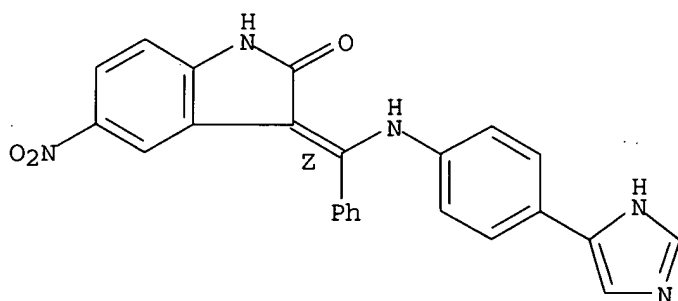
245546-28-5P 245546-29-6P 245546-32-1P
245546-33-2P 245546-34-3P 245546-35-4P
245546-36-5P 245546-37-6P 245546-39-8P
245546-45-6P 245546-46-7P 245546-47-8P
245546-48-9P 245546-50-3P 245546-57-0P
245546-65-0P 245546-68-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-(α -heteroarylaminobenzylidene)-2-indolinones as cyclin dependent kinase inhibitors)

RN 245545-75-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME).

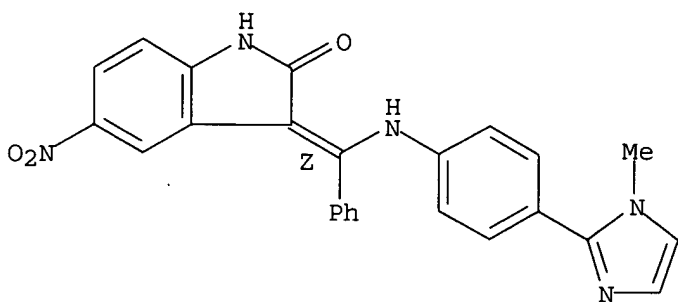
Double bond geometry as shown.



RN 245545-89-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

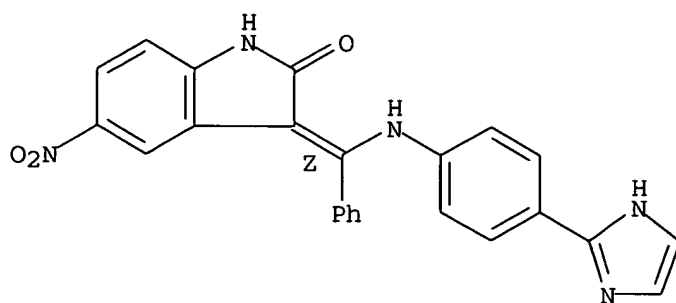
Double bond geometry as shown.



RN 245545-90-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

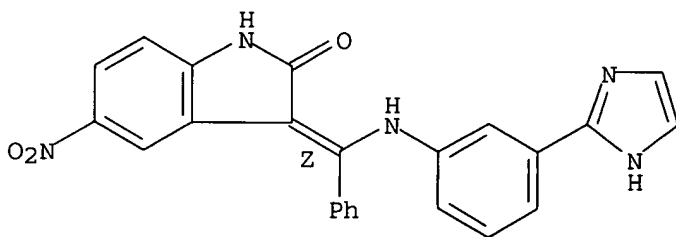
Double bond geometry as shown.



RN 245545-92-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[3-(1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

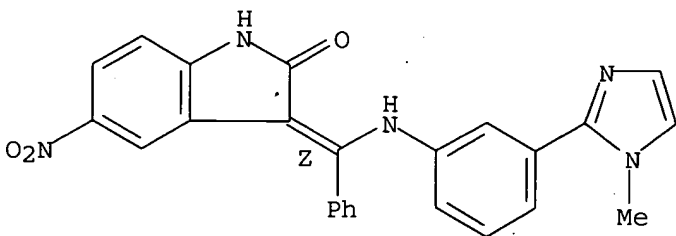
Double bond geometry as shown.



RN 245545-95-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[3-(1-methyl-1H-imidazol-2-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

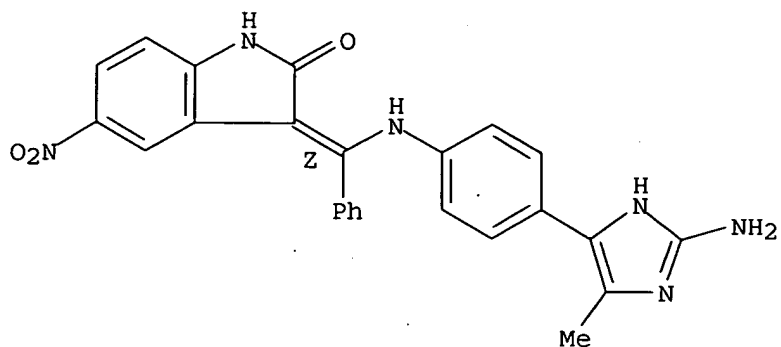
Double bond geometry as shown.



RN 245546-03-6 CAPLUS

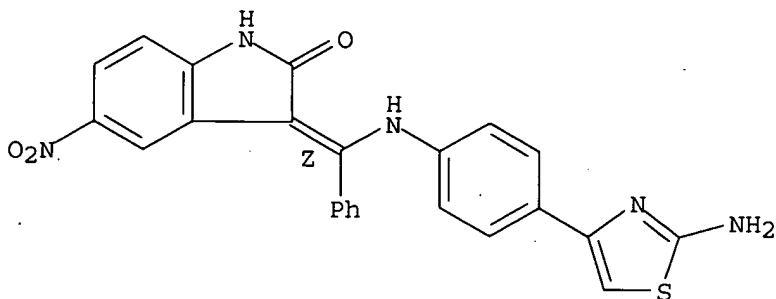
CN 2H-Indol-2-one, 3-[[[4-(2-amino-5-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



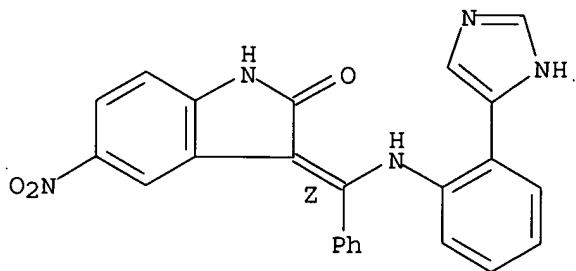
RN 245546-07-0 CAPLUS
 CN 2H-Indol-2-one, 3-[[[4-(2-amino-4-thiazolyl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



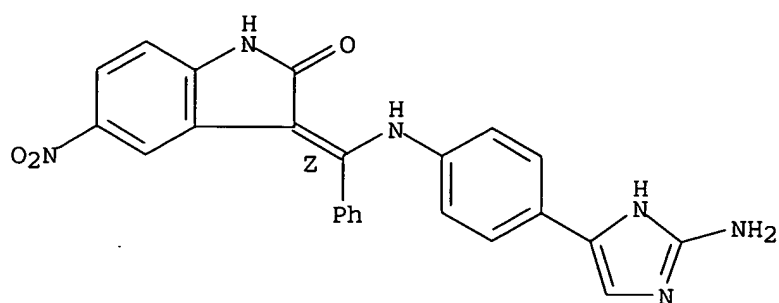
RN 245546-19-4 CAPLUS
 CN 2H-Indol-2-one, 1,3-dihydro-3-[[[2-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 245546-20-7 CAPLUS
 CN 2H-Indol-2-one, 3-[[[4-(2-amino-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

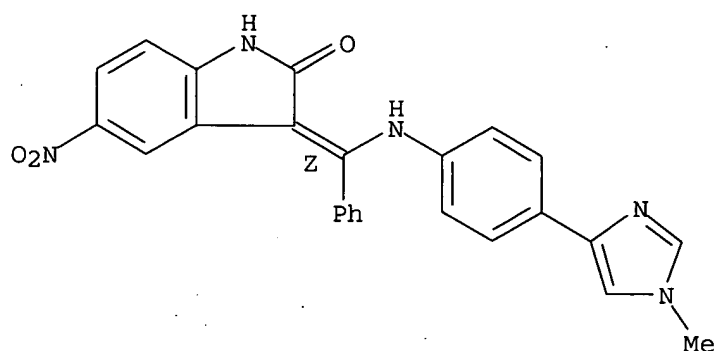
Double bond geometry as shown.



RN 245546-28-5 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

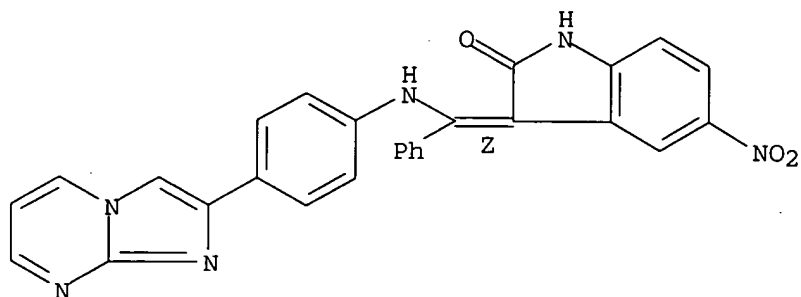
Double bond geometry as shown.



RN 245546-29-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-imidazo[1,2-a]pyrimidin-2-ylphenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

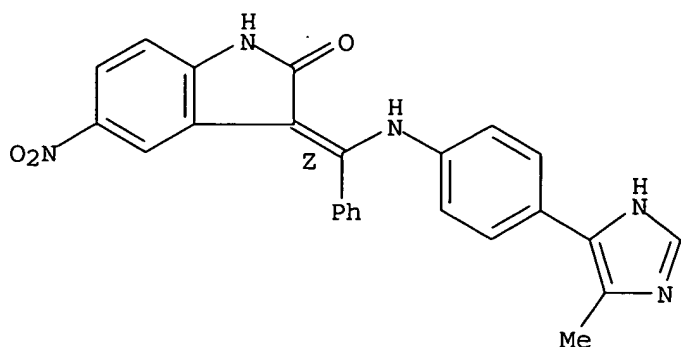
Double bond geometry as shown.



RN 245546-32-1 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(5-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

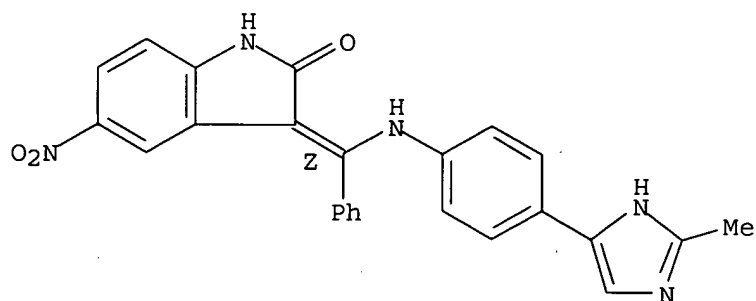
Double bond geometry as shown.



RN 245546-33-2 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(2-methyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

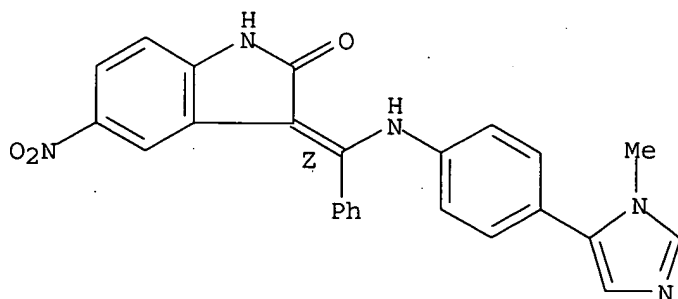
Double bond geometry as shown.



RN 245546-34-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1-methyl-1H-imidazol-5-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

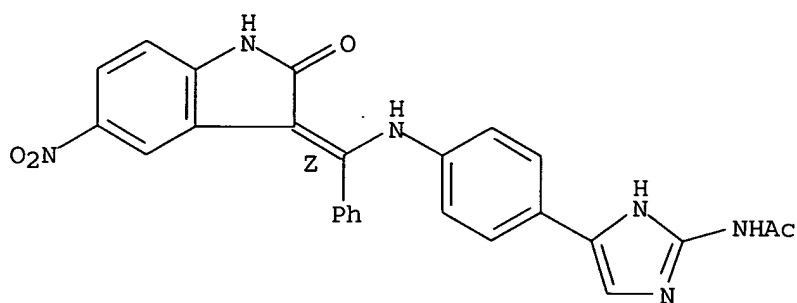
Double bond geometry as shown.



RN 245546-35-4 CAPLUS

CN Acetamide, N-[4-[4-[[[(Z)-(1,2-dihydro-5-nitro-2-oxo-3H-indol-3-ylidene)phenylmethyl]amino]phenyl]-1H-imidazol-2-yl]]- (9CI) (CA INDEX NAME)

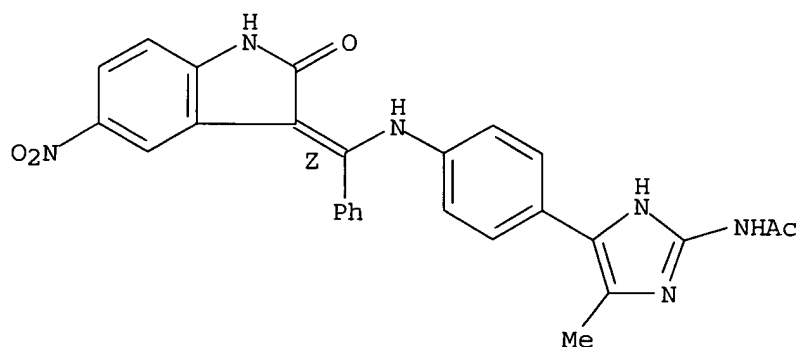
Double bond geometry as shown.



RN 245546-36-5 CAPLUS

CN Acetamide, N-[4-[4-[[(Z)-(1,2-dihydro-5-nitro-2-oxo-3H-indol-3-ylidene)phenylmethyl]amino]phenyl]-5-methyl-1H-imidazol-2-yl] - (9CI) (CA INDEX NAME)

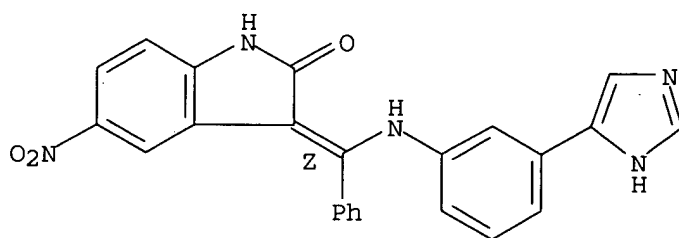
Double bond geometry as shown.



RN 245546-37-6 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[3-(1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

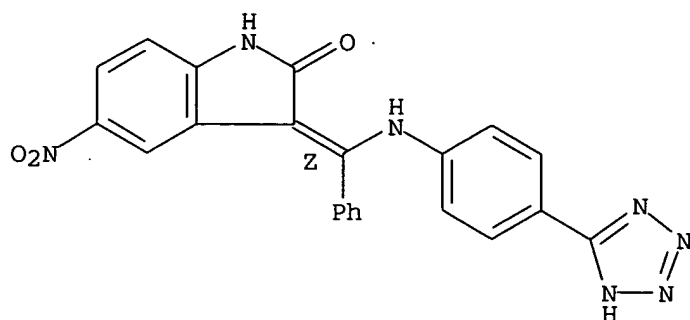
Double bond geometry as shown.



RN 245546-39-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-[phenyl[[4-(1H-tetrazol-5-yl)phenyl]amino]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

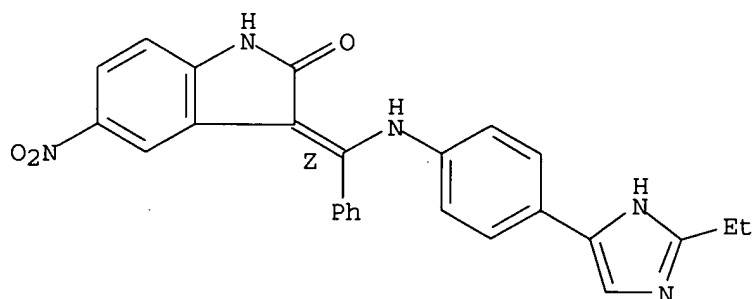
Double bond geometry as shown.



RN 245546-45-6 CAPLUS

CN 2H-Indol-2-one, 3-[[[4-(2-ethyl-1H-imidazol-4-yl)phenyl]amino]phenylmethylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

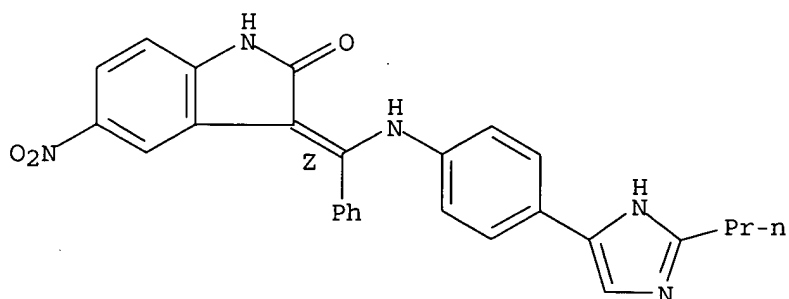
Double bond geometry as shown.



RN 245546-46-7 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-5-nitro-3-[phenyl[[4-(2-propyl-1H-imidazol-4-yl)phenyl]amino]methylene]-, (3Z)- (9CI) (CA INDEX NAME)

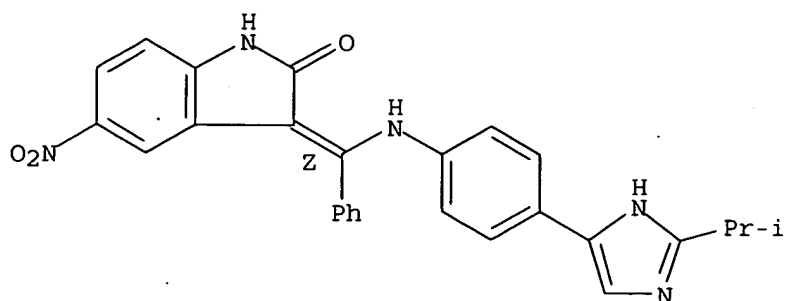
Double bond geometry as shown.



RN 245546-47-8 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-[2-(1-methylethyl)-1H-imidazol-4-yl]phenyl]amino]phenylmethylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

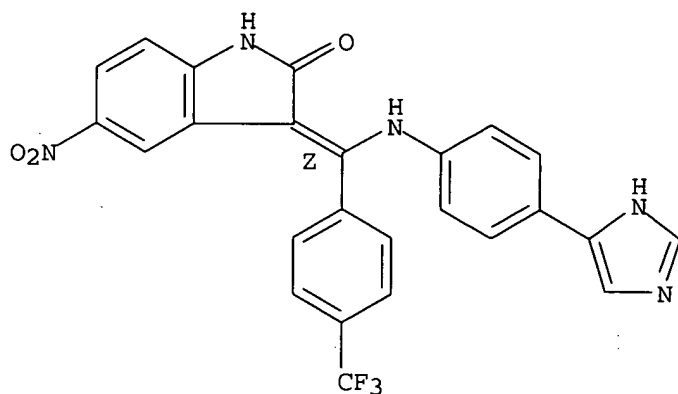
Double bond geometry as shown.



RN 245546-48-9 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino] [4-(trifluoromethyl)phenyl]methylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

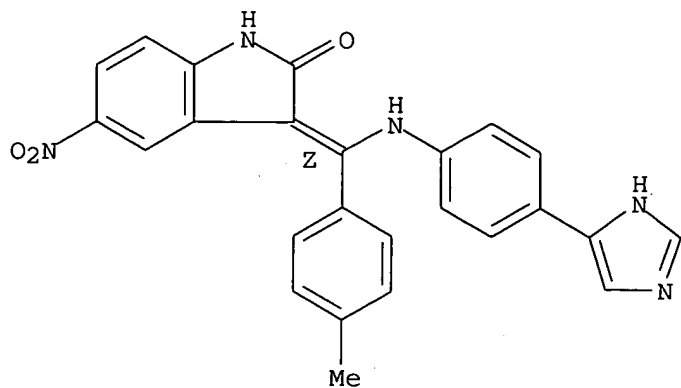
Double bond geometry as shown.



RN 245546-50-3 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-yl)phenyl]amino] (4-methylphenyl)methylene]-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



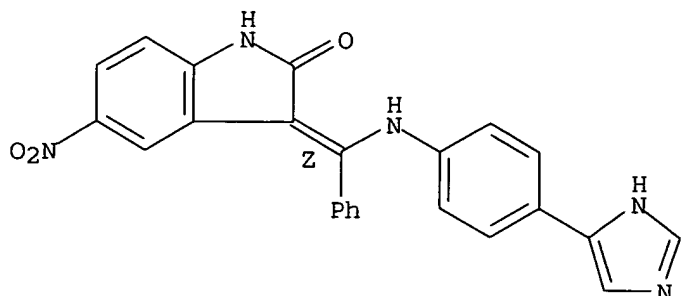
RN 245546-57-0 CAPLUS

CN 2H-Indol-2-one, 1,3-dihydro-3-[[[4-(1H-imidazol-4-

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yl)phenyl]amino]phenylmethylene]-5-nitro-, monohydrochloride, (3Z)- (9CI)
(CA INDEX NAME)

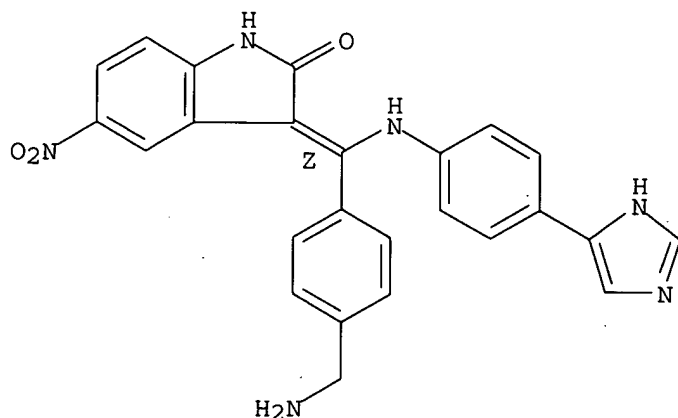
Double bond geometry as shown.



● HCl

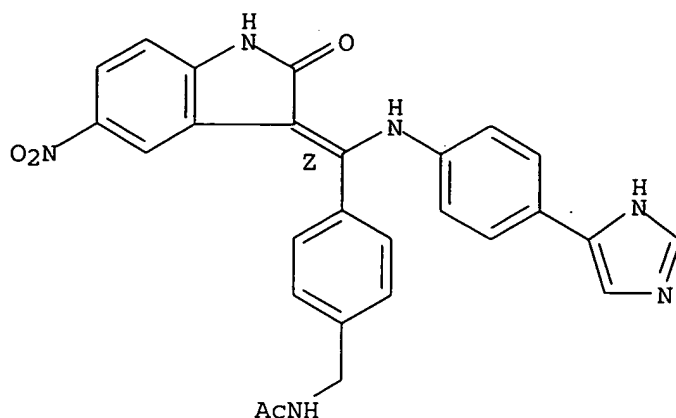
RN 245546-65-0 CAPLUS
CN 2H-Indol-2-one, 3-[[4-(aminomethyl)phenyl][[4-(1H-imidazol-4-yl)phenyl]amino]methylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 245546-68-3 CAPLUS
CN Acetamide, N-[[4-[(Z)-(1,2-dihydro-5-nitro-2-oxo-3H-indol-3-ylidene)[[4-(1H-imidazol-4-yl)phenyl]amino]methyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 245547-10-8P

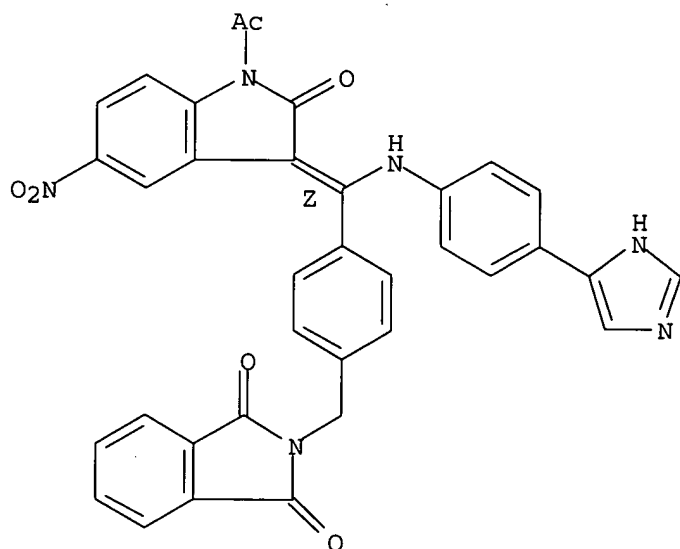
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 3-(α -heteroarylaminobenzylidene)-2-indolinones as cyclin dependent kinase inhibitors)

RN 245547-10-8 CAPLUS

CN 2H-Indol-2-one, 1-acetyl-3-[[4-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl][[4-(1H-imidazol-4-yl)phenyl]amino]methylene]-1,3-dihydro-5-nitro-, (3Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



=> log y

COST IN U.S. DOLLARS

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

ENTRY

93.92

TOTAL

SESSION

581.13

SINCE FILE

ENTRY

TOTAL

SESSION

06/20/2005 10783325.trn

CA SUBSCRIBER PRICE

-20.44

-20.44

STN INTERNATIONAL LOGOFF AT 11:47:48 ON 20 JUN 2005